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LONDON SATURDAY DECEMBER 5 1953

AN EPIDEMIOLOGICAL STUDY OF RHEUMATOID ARTHRITIS ASSOCIATED WITH CHARACTERISTIC CHEST X-RAY APPEARANCES IN COAL-WORKERS

BY

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[WITH SPECIAL PLATE]

A new syndrome has been described in coal-workers (Caplan, 1953) in which rheumatoid arthritis is associated with nodular fibrosis of the lung which is radiologically similar to, but distinguishable from, the massive fibrosis appearing in complicated pneumoconiosis. A syndrome which describes an association between two pathological conditions affecting different parts of the body is usually founded on a clinical impression but is rarely studied by epidemiological methods. Such methods may determine whether the association is more than a chance occurrence of the two conditions in the same subject. This paper describes an epidemiological study of rheumatoid arthritis in a community of coal-miners in South Wales to investigate this new syndrome.

Characteristic Chest X-ray Appearances

The radiological features of progressive massive fibrosis (P.M.F.) in coal-workers' pneumoconiosis have been fully described (Fletcher *et al.*, 1949). At the beginning, ill-defined opacities develop upon a background of category 2 or 3 simple pneumoconiosis; these gradually enlarge over a period of several years to produce irregular shadows which usually become more clearly defined; ultimately the masses may occupy most of a lobe and may be associated with distortion of surrounding structures and accompanied by emphysema. An example of the early stages of the development of such a shadow is shown in Fig. 1 (see Special Plate), and a typical example of advanced massive fibrosis is shown in Fig. 2.

The type of chest lesions associated with rheumatoid arthritis in miners is strikingly different in some respects. There is a much more rapid development of numerous discrete rounded opacities scattered diffusely throughout both lung fields. These lesions seem to appear in crops, the lesions in each crop being similar in size and rate of development. Over a period of a few months they attain a diameter of 1–2 cm., occasionally as large as 5 cm., and thereafter as a general rule they change relatively little over a period of years; they may gradually enlarge, and cavitation may occur in them; occasionally they contract to form stellate scars or they may calcify. Characteristically these lesions develop upon a background of less simple pneumoconiosis than does typical P.M.F.: whereas P.M.F. rarely, if ever, starts when there is less than category 2 simple pneumoconiosis, these "rheumatoid" lesions are often seen with a background of only category 1. Fig. 3 illustrates a typical example of the "rheumatoid" type of chest *x*-ray picture in a coal-miner aged 40 with a history of rheumatoid arthritis for the past eleven years. The *x*-ray appearances described above have been noted only in men exposed to a dust hazard and have no similarity to the interstitial pneumonitis occurring in cases of rheumatoid arthritis described by Ellman and Ball (1948).

Planning of the Investigation

The chest *x*-ray films used in this study were all of miners or ex-miners examined in the Rhondda Fach, a South Wales mining valley where over 95% of the mining and ex-mining population had been *x*-rayed (Cochrane *et al.*, 1952). In 896 cases these films had previously been classified as showing either P.M.F. (788) or clinically significant tuberculosis (108): from this group Caplan, as the first observer of the syndrome, selected all films showing the radiological appearances which he thought would be associated with rheumatoid arthritis. Twenty such films were selected. These 20 cases and a randomly selected group of 60 controls,

stratified by age and chosen from the miners whose films had been read and discarded as showing none of the characteristic appearances, were visited at their homes by a physician who was not aware of the *x*-ray findings. When visiting these men, a standard questionary was used and all joints of the arms and legs were examined in cases in which the history suggested arthritis.

To check the reproducibility of reading the chest films, all 896 films were re-read by the same observer, and to determine the inter-observer error of diagnosis of rheumatoid arthritis in field-survey work another physician visited all selected cases and any controls who had shown some evidence of rheumatoid arthritis. This small study of intra- and inter-observer error is described in the Appendix.

All men considered by either physician to have rheumatoid arthritis, and the 20 cases selected because of their characteristic chest *x*-ray films, were more fully investigated later. A positive diagnosis of rheumatoid arthritis was made only when at least two of the following criteria were satisfied: (1) A typical history of symmetrical polyarthritis with or without residual deformity; (2) characteristic changes of rheumatoid arthritis in the *x*-ray films of hands or feet; and (3) a positive differential agglutination test for rheumatoid arthritis (Rose *et al.*, 1948).

In this investigation we were particularly keen to miss no cases of rheumatoid arthritis, and as a consequence several of the men considered to be doubtfully positive when seen at their homes when investigated further either failed to fulfil the criteria or were proved to be suffering from some other arthritic condition.

Results

Prevalence of Rheumatoid Arthritis

The proportion of cases of rheumatoid arthritis found among the control group of cases of P.M.F. or tuberculosis (3%) was greater than that reported in the normal population. In the Sickness Survey (Stocks, 1949) a prevalence of 0.419% among all males and females over the age of 16 was found, and in a recent investigation of rheumatism in coal-miners in Lancashire, Lawrence and Aitken-Swan (1952) reported less than 1% of cases in the same age groups, suggesting that the prevalence of this disease among miners is no higher than in the general population, but it should be noted that massive fibrosis itself is probably less common in Lancashire than in South Wales (unpublished data, Pneumoconiosis Research Unit).

As a higher prevalence of rheumatoid arthritis was found among cases of massive fibrosis than had been expected, it was clearly necessary to determine its prevalence in miners with and without simple pneumoconiosis, and two further groups were selected in the same way as the group with P.M.F. Several doubtfully positive cases in these other *x*-ray groups were also fully investigated, but with negative results. Table I shows the prevalence of rheumatoid arthritis in the four *x*-ray groups visited.

The prevalence is very much higher in the group with characteristic chest *x*-ray films than in any of the other three groups. Indeed, in these cases the diagnosis of rheumatoid arthritis could have been made from the chest *x*-ray films alone with more than a 50% chance of being correct. The prevalence of this type of arthritis also seems to be greater in cases of P.M.F. than in miners with simple pneumoconiosis or with chest *x*-ray films which show no signs of pneumoconiosis.

Table II is a summary of the clinical and *x*-ray findings of the 20 cases with characteristic *x*-ray appearances and of the two cases in the P.M.F. group, and shows those who were proved to be suffering from rheumatoid arthritis. It was found that there was no close correlation beween the more typical "rheumatoid" chest *x*-ray film and the activity, severity, and time of onset of arthritis, or between the chest *x*-ray films and the radiological evidence of rheumatoid arthritis in the hands and feet. The analysis by age, dust exposure, and somatotype does, however, reveal some points of interest.

TABLE I.—*Prevalence of Rheumatoid Arthritis Among Miners and Ex-miners, Analysed by Chest X-ray Appearances*

Clinical Findings	Chest *X*-ray Groups			
	Characteristic "Rheumatoid" Lesions	Progressive Massive Fibrosis or Clinically Significant Tuberculosis	Simple Pneumoconiosis	Normal
Proved rheumatoid arthritis	11 (55%)	2 (3%)	—	—
No rheumatoid arthritis ..	9 (45%)	57 (97%)	92	112
Total ..	20 (100%)	59* (100%)	92	112

The difference between those with characteristic rheumatoid chest *x*-ray films and the control group of P.M.F. is highly significant. The difference in incidence between the P.M.F. group and the simple pneumoconiosis and normal group is exactly at the 5% level of significance.

* One patient in this group had died in the interval between the *x*-ray survey and this investigation.

(a) Age.—The mean age of men with typical "rheumatoid" chest *x*-ray films and with arthritis was 48.9 years, compared with 41.5 years for those with similar chest films but without arthritis. This difference is not statistically significant ($0.10<P<0.20$). The "rheumatoid" lung lesions may precede the onset of arthritis by several years, as is discussed later, and it is possible that a number of men with typical *x*-ray films and without arthritis may develop it at a later date. The average age of onset of arthritic symptoms among the proved cases was 41.7 years.

(b) Total Dust Exposure.—The total duration of dust exposure has a mean of 22.6 years in the proved cases, as opposed to 16.3 years in those without arthritis. This difference is statistically significant ($0.01<P<0.02$). Age and total length of exposure to dust are of course correlated, and by making allowance for this fact it should be possible to throw some light on which is more closely related to the arthritis. The mean age of the proved rheumatoid arthritis cases can be compared with that of those without arthritis when the length of dust exposure has been allowed for, and, similarly, the duration of dust exposure standardized for age can be compared in the two groups. When this is done there is no significant difference between the two groups either in age ($0.60<P<0.70$) or in dust exposure ($0.10<P<0.20$), but whereas length of dust exposure, which previously was significant, now becomes just less than significant, all suggestion of a difference in age has vanished. Thus the dust exposure might be a factor differentiating the two groups, and age probably only so far as it is related to dust exposure. This difference, however, is not established with any degree of confidence.

(c) Stone Dust Exposure.—When analysed according to years of exposure to stone dust some interesting results are forthcoming. Taking the group with characteristic "rheumatoid" *x*-ray films and the control group of P.M.F. cases, we find there is no statistically significant difference between their exposure to stone dust, though it is possible that such a difference is present but not revealed in these relatively small groups. In the group with typical "rheumatoid" *x*-ray films, however, there are nine men who have had exposure to stone dust, and seven of these occur in the group of eleven who have proved rheumatoid arthritis. Two occur in the group without arthritis. The probability of this occurring fortuitously is 8%. Of these nine men, five have had a stone dust exposure of three years or more, and all these have rheumatoid arthritis. The probability of this occurring fortuitously is only 3%. The significance, if any, of this curious finding will be determined only when further cases of this syndrome are investigated. It is of interest to note that Collis and Yule (1933),

TABLE II.—*Summary of Clinical Findings and Industrial Histories of 20 Cases with "Rheumatoid" Chest X-ray Films and 2 Cases with P.M.F.*

No.	Age (Years)	History of Rheumatoid Arthritis	Differential Agglutination Test (Rose)	X-ray Diagnosis of Rheumatoid Arthritis: Hands, Observer A*	Hands, Observer B*	Feet, Observer A	Feet, Observer B	Lowest E.S.R. (Westergren) mm. Fall in 1 Hour	Middlebrook–Dubos Agglutination Test (1:8 positive)	Somatotype Index	Age of Onset of Arthritis (Years)	Years of Dust Exposure Before X-ray: Stone	Stone and Coal	Coal	Total
Cases with Proved Rheumatoid Arthritis with "Rheumatoid" Chest X-ray Films															
1	72	+	+	3	3	3	3	40	–	107·8	47	—	—	34	34
2	60	+	+	2	2	2	2	36	+	114·4	58	8	—	26	34
3	58	+	–	1	2	2	2	39	–	99·4	48	—	—	22	22
4	50	+	–	1	1	0	0	30	–	111·5	45	3	—	19	22
5	49	+	+	1	0	0	0	6	+	105·3	47	18	—	9	27
6	46	+	–	0	1	0	1	20	N.R.	108·9	44	—	1	25	26
7	43	+	+	1	1	2	2	5	+	108·6	37	3	—	11	14
8	41	+	+	0	0	0	0	16	–	104·3	39	—	2	17	19
9	40	+	+	0	1	0	0	13	+	100·5	38	—	—	19	19
10	40	+	+	1	1	2	2	21	+	113·7	29	—	—	15	15
11	39	+	+	0	1	2	2	14	–	95·3	27	—	12	5	17
	Mean 48·9		72·7% positive					Mean 21·8	50% positive	Mean 106·3	Mean 41·7				Mean 22·6 yrs.
Cases without Proved Rheumatoid Arthritis with "Rheumatoid" Chest X-ray Films															
12	50	–	–	0	0	0	0	30	–	99·3	—	—	—	23	23
13	48	+(?)	–	0	0	0	0	23	+	98·7	47(?)	—	—	15	15
14	45	–	–	0	0	0	0	4	–	105·5	—	—	—	20	20
15	44	–	–	0	0	0	0	7	+	111·7	—	—	—	20	20
16	40	–	–	0	0	0	0	1	–	105·6	—	—	2	12	14
17	39	–	–	0	0	0	0	6	–	99·4	—	—	—	13	13
18	38	–	–	0	0	0	0	5	+	105·3	—	1	—	19	20
19	35	–	–	0	1	0	0	56	–	100·0	—	—	—	10	10
20	35	–	N.R.	0	0	0	0	N.R.	N.R.	102·4	—	—	—	12	12
	Mean 41·5							Mean 16·5	37·5% positive	Mean 103·1					Mean 16·3 yrs.
Cases with Proved Rheumatoid Arthritis with P.M.F. Chest X-ray Films															
1	41	+	+	2	2	2	2	85	–	93·8	30	—	4	8	12
2	49	+	+	1	1	2	2	5	–	94·0	48	—	—	26	26

The readings of the *x*-ray films of the hands and feet are scored as follows: 0=normal or doubtful changes of rheumatoid arthritis; 1=minimal changes of rheumatoid arthritis; 2=moderate changes of rheumatoid arthritis; 3=marked changes of rheumatoid arthritis. N.R.=no record.
* Observers A and B, see Appendix.

who analysed the Registrar-General's Decennial Supplement for 1921–3, found a remarkably increased mortality from a wide range of diseases in men exposed to a silica risk. This included a fourfold increase in the mortality rate from chronic rheumatic conditions.

(d) Somatotype.—It is often said that rheumatoid arthritis affects people of asthenic build. In this series anthropometric measurements were made, using the body index suggested by Rees and Eysenck (1945), which is

$$\frac{100 \times \text{stature in cm.}}{6 \times \text{mean chest diameter in cm.}}$$

Analysis shows that the group with typical "rheumatoid" chest *x*-ray films but without arthritis are similar in body build to the control cases with P.M.F., but those with arthritis have a higher mean "body index"—that is, they are of a more asthenic type. This difference may be a sampling effect, but if it is justifiable to assume that all the cases with typical "rheumatoid" chest films have some factor predisposing to the development of arthritis (see under Discussion) then this predisposing factor is not related to somatotype, and the difference in body build is probably secondary to the rheumatoid arthritis.

Clinical Investigations

Clinical examination, the *x*-ray appearances of peripheral joints, the erythrocyte sedimentation rate, and the differential agglutination test all indicated that the type of arthritis seen in these miners differs in no way from rheumatoid arthritis in other people. Of the 12 men who gave histories suggestive of rheumatoid arthritis, positive differential agglutination tests were obtained in eight. No positive result was obtained in any case without a history of polyarthritis. These findings agree with those found in other series of rheumatoid arthritis in males, and would not be expected in other arthritic conditions, with the possible exception of disseminated lupus erythematosus (Ball, 1952).

The Middlebrook–Dubos agglutination test was also carried out. This test, which is based on the agglutination by tuberculous patients' serum of sheep's red cells sensitized to tuberculin, seems to be of limited value except in research into the pathogenesis of tuberculosis, the false positives and false negatives being so numerous that the significance of the result in any individual case cannot be determined. In this series we found 8 positive results (agglutination to a titre of 1:8) in 18 sera tested (44%). In a series of 133 cases of early progressive massive fibrosis, agglutination to a titre of 1:8 occurred in only four cases (3%). This suggests that the lesions in the lungs are a form of tuberculosis, and there is other evidence which supports this, but both the Middlebrook–Dubos and the Rose agglutination test are based on the agglutination of sensitized sheep's cells by human serum, and may be interrelated.

Sputa or laryngeal swabs were cultured for tubercle bacilli in all cases, but there was only one positive (No. 8), and in his case morphologically atypical tubercle bacilli were isolated, which, however, produced tuberculosis on guinea-pig inoculation.

One man of 72 years (Case 1) has died since this investigation was made. His arthritis dated from 1926 and caused him to leave coal-mining in 1928 after having worked 25 years underground, chiefly as a collier. The significant clinical findings are shown in Table II, and *x*-ray films of his chest and hands are shown in Figs. 4 and 5. A summary of the post-mortem examination conducted by Dr. D. Rivers is given below.

Post-mortem Findings in Case 1

External Appearances.—The body was that of a well-nourished elderly male with numerous coal-pigmented scars present on the hands and forearms and pitting oedema of the lower limbs. Characteristic periarticular swellings and gross deformities of rheumatoid arthritis were present in the elbows, wrists, knees, and ankles. There was subluxation and severe ulnar deviation at all metacarpo-phalangeal joints

of the left hand, with spindling of the proximal interphalangeal joints; the right hand showed much less deformity, but changes typical of severe rheumatoid arthritis. The small toes of both feet had been amputated and there was pronounced lateral deviation of both large toes. No rheumatoid nodules were present.

Internal Appearances.—Pleural adhesions were present in both sides of the chest. Both lungs were enlarged and there was some bullous emphysema at the apices and along the free margins. The cut surface of the right lung showed a group of circumscribed fibrous nodules in the apex of the upper lobe, some of which were joined by narrow bands of black fibrous tissue. These fibrous lesions were 1–2 cm. in diameter, were almost entirely black in colour, but had a whorled appearance formed by thin concentric laminae of yellowish-white fibrous tissue. A number of similar lesions were scattered throughout the rest of the lung, and in addition there were numerous small dust-pigmented fibrous nodules varying from 1 to 2 mm. in diameter. Most of both the larger and the smaller lesions showed central softening and necrosis, but there was no definite caseation or other evidence of tuberculosis. The left lung showed essentially similar appearances, and in the lower part of the upper lobe there was also a large mass of black dust-pigmented fibrosis measuring 5 cm. across its greatest diameter. Central softening and necrosis were present in this mass, but again there was no definite evidence of tuberculosis. Both lungs showed a moderate number of soft-coal-dust foci uniformly distributed throughout their parenchyma, and both were congested and oedematous. The mediastinal lymph nodes were enlarged, black, and firm. There was some cardiac enlargement with right ventricular hypertrophy and atheroma in the main pulmonary arteries and their smaller branches. The liver, spleen, and kidneys were very congested. All other organs appeared normal.

Microscopical Appearances.—The histological features of the predominant type of lung nodule were essentially similar. Each had a large amorphous eosinophilic centre with numerous cholesterol clefts, and in some of them patchy calcification was present. This zone was surrounded by dense collagenous fibrosis, the inner layers of which were hyalinized, and the ghost structure of collagen could be identified towards the periphery of the central zone. In some lesions this central zone consisted of completely hyalinized collagen. A large amount of coal dust was distributed beween the fibres of collagen and throughout the centres of the lesions.

Sections of the large mass in the left lung showed it to consist of largely hyalinized dense collagen containing areas of eosinophilic necrosis and cholesterol clefts and heavily impregnated with coal dust. No definite histological evidence of tuberculosis was identified in sections of the nodules or the mass, and no acid-fast bacilli could be found in Ziehl–Neelsen preparations.

Comment.—The cause of death was considered to be congestive cardiac failure due to coal-workers' pneumoconiosis. Though the macroscopical and microscopical appearances of the individual lung lesions are often seen in cases of P.M.F., and the rounded nodules are similar to those described by Gough (1947) as infective nodules, it is unusual to find them so large, so sharply circumscribed, or so numerous and widely distributed as in this case. The pathological evidence supports the contention that the lesions are unlikely to differ in aetiology from that of P.M.F., but material from a case in the active phase is essential to establish this more firmly. It is probable that the lesions described here were active about the time of onset of this man's arthritis 27 years ago, and the appearances are now those of a completely healed infection.

Discussion

This investigation has confirmed the observation that a particular type of radiological appearance in the chest *x*-ray films of coal-miners is closely associated with the presence of rheumatoid arthritis.

P.M.F. in coal-workers is generally regarded as tuberculosis modified by the presence of coal dust (Gough, 1947; Fletcher, 1948). How do these typical "rheumatoid" lung lesions differ from ordinary P.M.F.? The pathology of this syndrome has been studied at necropsy in only one radiologically characteristic case, but necropsies have recently been performed on seven cases of rheumatoid arthritis in coal-workers with chest films similar to, but less typical than, those described in this series, and evidence of active tuberculosis was found in five of them. The only two men with "rheumatoid" lung lesions who have had a positive sputum culture in life were noted to have morphologically atypical bacilli which, however, produced tuberculosis in guinea-pigs on inoculation.

In spite of the two types of lung lesions tending to merge into one another, we can say in general of the "rheumatoid" lesions that from the radiological point of view there is comparatively little simple pneumoconiosis relative to the time of appearance of the lesions; from the industrial point of view exposure to stone-dust inhalation seems important; from the bacteriological point of view the tubercle bacilli may be abnormal; and from the pathological point of view the lesions are individually similar to the infective nodules commonly found in the neighbourhood of the fibrotic masses of P.M.F. but are larger, more numerous, more discrete, and more widespread than are usually seen in complicated pneumoconiosis.

We have reported here only the results of an investigation in one mining valley, but a number of other cases of this syndrome have been studied. One most interesting finding concerns the time relationship between the development of rheumatoid arthritis and the development of the characteristic "rheumatoid" chest *x*-ray appearances. It seems likely that in most cases the onset of arthritic symptoms coincides with the development of the lung lesions. In some cases, however, the characteristic *x*-ray appearances may precede the arthritis by several years, and one case has been found of a miner who developed rheumatoid arthritis six years before his first chest *x*-ray film was taken; this showed simple pneumoconiosis. The next film, taken five years later, showed the typical "rheumatoid" appearances.

It has been shown that there is probably an increased prevalence of rheumatoid arthritis among cases of P.M.F. On the evidence available it is not possible to state whether the P.M.F. predisposes to rheumatoid arthritis, or whether rheumatoid arthritis predisposes to P.M.F., or whether the factors predisposing to rheumatoid arthritis also predispose to P.M.F. This problem can only be investigated epidemiologically by determining the attack rates of rheumatoid arthritis in men with and without massive fibrosis. It is nevertheless of interest to seek an explanation of the association of rheumatoid arthritis with these characteristic "rheumatoid" lung lesions, and there are at least three possible explanations of this association.

1) The simplest hypothesis is that the changes in the lung are merely one manifestation of the rheumatoid syndrome and are unrelated to typical P.M.F. Kellgren (1952) has suggested that the inflammatory lesion in the connective tissues in rheumatoid arthritis may be due to collagen breakdown, and it is possible that such changes in the lungs would be made more radio-opaque by the migration of dust-laden phagocytes to these areas of inflammation. This hypothesis is possible, but it is improbable for the following reasons: (*a*) Such lesions, even if less obvious, would have been seen at necropsy in non-miners. (*b*) There is some clinical and post-mortem evidence that the lesions are tuberculous. (*c*) Similar radiological findings have never been reported in association with rheumatoid arthritis. No similar cases were found among non-miners in the Rhondda Fach scheme, where almost 90% of the adult population of 20,000 people were *x*-rayed (Cochrane *et al.*, 1952).

2) Discarding the first hypothesis, then, the second explanation of the association is that the pathological changes reflected in the *x*-ray film may play the part of a chronic septic focus, one of the many other postulated factors in the

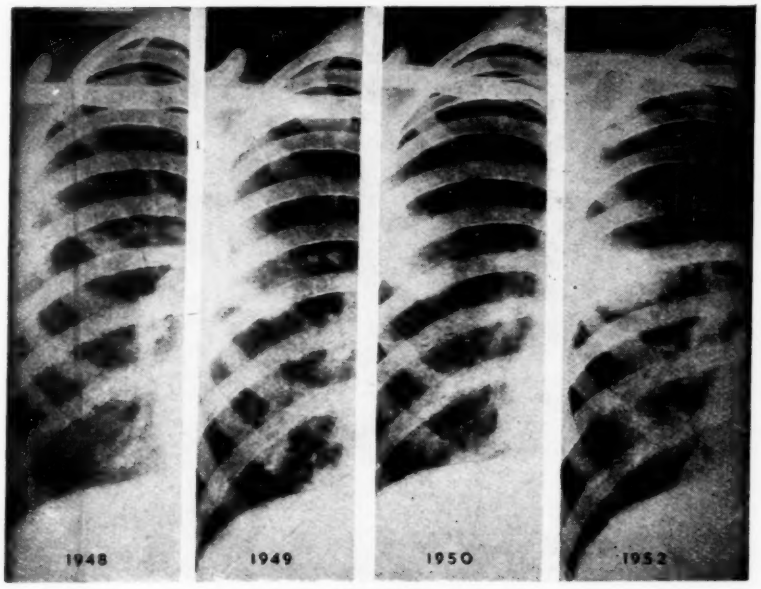

FIG. 1

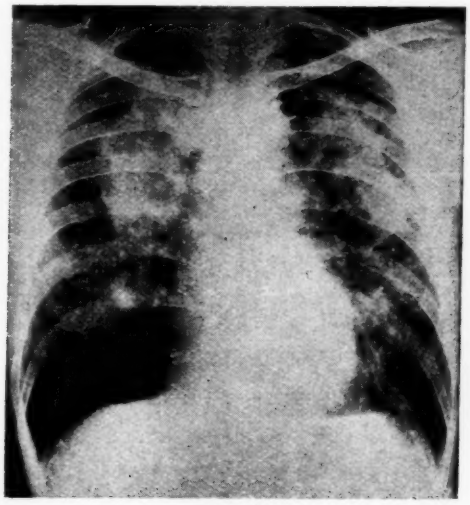

FIG. 2

FIG. 1.—The gradual development of a typical massive fibrosis opacity in the right mid-zone.

FIG. 2.—A typical example of advanced massive fibrosis.

FIG. 3.—A typical example of "rheumatoid" appearances.

FIG. 4.—Coal-miner aged 72 (Case 1) with rheumatoid arthritis of 26 years' duration.

FIG. 5.—Same case as Fig. 4, showing advanced changes of rheumatoid arthritis in both hands.

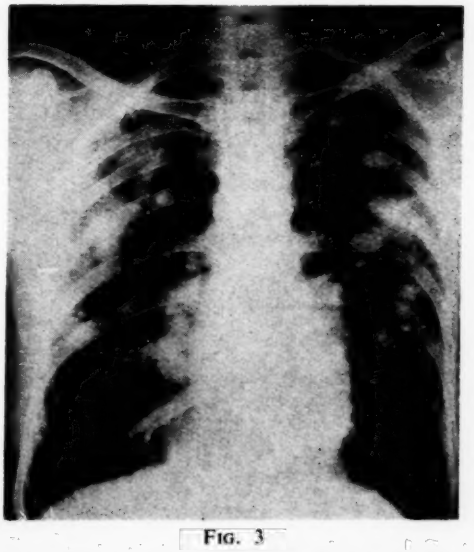

FIG. 3

FIG. 5

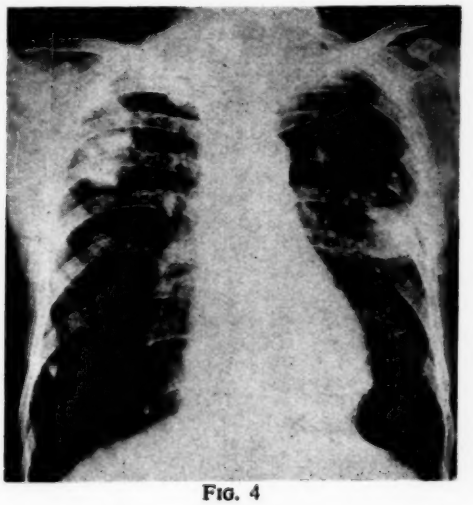

FIG. 4

FIG. 1.—Infant femur (×3). Inferior aspect of head and neck, showing anastomosis between anterior and inferior retinacular vessels.

FIG. 2.—Posterior view of femoral neck. Arteries injected, and black paper under pedunculated retinaculum.

FIG. 3.—Postero-inferior retinaculum from below.

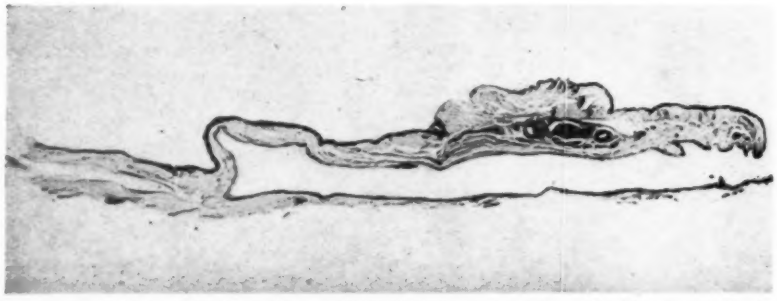

FIG. 4.—Section of retinaculum and periosteum of neck, with blood vessels in pedicle. (×3.)

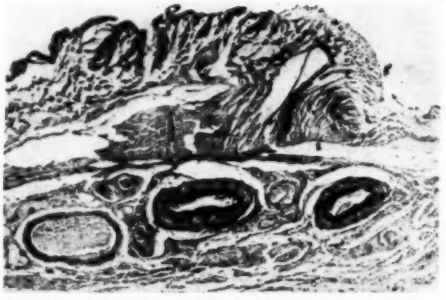

FIG. 5.—Vascular region, showing two thick-walled arteries and one vein. (×18.)

FIG. 6.—Injected retinacular artery to epiphysial centre and recurrent branches to juxta-epiphysial region. (×2.)

FIG. 7.—Indian ink injection showing increased concentration of blood vessels at the juxta-epiphysial "line." (×4¼.)

FIG. 8.—Skiagram of femoral segment, illustrating the superior and inferior triangles at the junction of head and neck.

aetiology of rheumatoid arthritis. Against this hypothesis we have the fact that in one case the arthritis preceded the development of typical "rheumatoid" lung lesions by more than six years, and in other cases there may be a latent period of as much as 11 years between the development of the typical lung lesions and the onset of arthritis.

It is possible, therefore, that neither of these hypotheses is correct and that there is some other factor which is causally related to both the arthritis and this type of "rheumatoid" lung lesion—for example, a more fundamental generalized abnormality of tissue reaction to dust and infection.

As these "rheumatoid" lung lesions in miners can develop several years before, concurrently with, or several years after the onset of arthritis, the suggestion is that there may be a particular type of tissue reaction to dust and tuberculosis in the lungs of miners who are predisposed to the development of rheumatoid arthritis. Recent work on adrenal cortical hormones and their relationship to rheumatoid arthritis and to tissue reaction suggests that this may be part of the explanation.

A.C.T.H. and cortisone are known to diminish the inflammatory response to trauma and chemical irritants (Shapiro *et al.*, 1951), to diminish the tuberculin reaction (Long and Miles, 1950; Long *et al.*, 1951; Pickering, 1952), and to inhibit the migration of dust cells in animals receiving intratracheal injection of powdered quartz (Harrison *et al.*, 1952). The formation of silicotic granulomata after intraperitoneal injection of powdered quartz is inhibited or diminished by cortisone in some experimental animals (Magarey and Gough, 1952; Schiller, 1953). These are the effects of excess A.C.T.H. and cortisone. Methods of assaying the levels of circulating A.C.T.H. and cortisone are not yet sufficiently developed to indicate whether these hormones are diminished in cases of rheumatoid arthritis; but Venning, Johnson, and Rose (1951) demonstrated a lowered excretion of certain groups of adrenal steroids in cases of rheumatoid arthritis, and Pearse (1950) found pituitary changes in patients dying with active rheumatoid arthritis, which he considered secondary to adrenal dysfunction. It is possible that rheumatoid arthritis may be related to adrenal or pituitary function, but, as Pickering (1952) points out, there is apparently no increased prevalence of this condition in cases of Addison's disease and Simmonds's disease, and it is therefore unlikely that it is simply due to a pituitary or adrenal defect; but such a defect may contribute to its aetiology, and, similarly, may contribute to the type of tissue reaction causing these "rheumatoid" lung lesions.

Summary

An epidemiological investigation of a syndrome in which rheumatoid arthritis is associated with characteristic chest *x*-ray appearances in coal-workers is described.

The widespread nodular fibrosis shown in these *x*-ray films is radiologically distinguishable from typical progressive massive fibrosis, but the available evidence suggests that the aetiology of both types of lesion is similar.

The prevalence of rheumatoid arthritis among cases with these characteristic chest *x*-ray films is over 50%; among cases of P.M.F. it was found to be 3%; whereas no cases were found in two similar groups of miners with and without simple pneumoconiosis.

The significant epidemiological, clinical, and pathological findings are given, and some possible explanations of the relationship between the "rheumatoid" lung lesions and the arthritis are discussed.

We wish to acknowledge our indebtedness to our colleagues in the Pneumoconiosis Research Unit for much helpful criticism and advice, and particularly to Dr. J. C. Gilson, the director; to Drs. C. M. Fletcher and R. F. Mahler, until recently members of the Unit; and to Dr. D. Rivers, who supplied the report on the pathology of this syndrome. The *x*-ray films of the peripheral joints were kindly read for us by Dr. J. H. Kellgren and Dr. J. Sharp, of the Manchester Rheumatism Research Centre; the differential agglutination tests were performed by Dr. J. Ball, of the same unit; and the Middlebrook–Dubos tests were carried out by Dr. Geraint James and Dr. F. O'Grady at the Middlesex Hospital. It is a pleasure to record our thanks to them, and to the miners who so willingly co-operated in this survey.

APPENDIX

(a) Intra-observer Error in Reading Characteristic Chest X-ray Appearances.—All 896 films were read twice by the same observer. On the first occasion 20 films were selected as showing these typical appearances and divided into four groups—A, B, C, and D—group A being the most typical, group D the least typical. On the second occasion 27 films were selected, and divided in three groups only—A+B, C, and D. On the second reading, 16 of the 20 original films were reselected; only one of the four cases not reselected on this occasion was a proved case of rheumatoid arthritis, but 11 new cases not previously selected were added in this group; clinically none of these was a case of rheumatoid arthritis, but none was fully investigated in hospital. Of the 16 selected on each occasion, 13 were allotted to the same subgroups as previously. These results are shown in Table III.

TABLE III.—*Intra-observer Error in Reading "Rheumatoid" Chest X-ray Films in Miners*

	"Rheumatoid" Chest X-ray Appearances	Second Reading: A and B	C	D	Not Selected on Second Reading	Total
First reading	A and B ..	5	1	—	—	6
	C	1	6	—	2*	9
	D	—	1	2	2	5
	Not selected on first reading	—	4†	7†		
	Total ..	6	12	9		

Cases selected on first reading were all fully investigated.
* One of these cases had proved rheumatoid arthritis, the other three not selected on second reading were not suffering from rheumatoid arthritis.
† These 11 cases selected on second reading but not selected on first reading all had no clinical evidence of rheumatoid arthritis, but were not fully investigated in hospital.

(b) Intra-observer Error in Clinical Diagnosis of Rheumatoid Arthritis under Field-survey Conditions.—Two observers visited cases at an interval of about three months. In this study 20 men with characteristic *x*-ray films and 5 men without characteristic *x*-ray films but thought by Observer A to be possible cases of rheumatoid arthritis were visited by both doctors. Table IV shows the result of this investigation. It will be seen that both observers agreed on the clinical grading of 20 of the 25 men, but both thought two were cases of rheumatoid arthritis when this diagnosis was not substantiated, and both thought one case normal when in fact he was suffering from rheumatoid arthritis. Observer A saw 16 cases he thought positive, of which 12 were later proved cases, and 9 he thought negative, of which 1 was later a proved case. Observer B saw 12 cases he thought positive, of which 10 proved to be so, and 13 cases he thought negative, of which 3 were later proved cases. Such disagreement as occurred

TABLE IV.—*Inter-observer Error in the Clinical Diagnosis of Rheumatoid Arthritis in the Field*

	Clinical Grade	Observer B: Certain	Probable	Possible	Negative	Total
Observer A	Certain ..	7 (7)	—	—	—	7 (7)
	Probable	1 (1)	3 (1)	—	—	4 (2)
	Possible..	—	—	1 (1)	4 (2)	5 (3)
	Negative	—	—	—	9 (1)	9 (1)
	Total ..	8 (8)	3 (1)	1 (1)	13 (3)	25 (13)

The numbers in parentheses indicate proved cases of rheumatoid arthritis.
Certain = Typical history + marked residual signs.
Probable = Typical history + minimal residual signs.
Possible = Typical history + no residual signs.

is partly explicable by the desire to find very early cases of a disease in which the earliest symptoms and signs are not usually clearly defined.

(c) Inter-observer Error in Reading Characteristic X-ray Changes of Rheumatoid Arthritis in the Hands and Feet.—Two observers from the Manchester Rheumatism Research Centre kindly read the films of the hands and feet of the 20 cases with typical "rheumatoid" chest *x*-ray films. Their readings are plotted against each other in Table V. In reading the films of the hands there was agreement in 13 of the 19 cases, but in 5 cases one observer noted changes (3 of which were osteoporotic changes only) which were not noted by the other observer; in the remaining case the difference was only one of degree. In reading the films of the feet, however, there was agreement in 18 of the 19 cases. Table V also indicates that the *x*-ray changes in the feet seemed less likely to be present than in the hands, but when present they were more severe. In this series, four cases of proved rheumatoid arthritis had no changes in the *x*-ray films of the feet, whereas only one case had no changes in the *x*-ray films of the hands; nevertheless, among these 11 cases of rheumatoid arthritis six had moderate or marked changes in the feet, whereas only two had moderate or marked changes in the hands. Typical *x*-ray changes of rheumatoid arthritis were never read by either observer in this series for any case which had no other clinical evidence of arthritis; there was one case of proved arthritis which both observers agreed had no *x*-ray changes in the hands or feet. This study would have been improved if a normal control bone had been used when each film was taken. Many films were read as "doubtful" because osteoporosis cannot be accurately assessed without such a control.

TABLE V.—*Inter-observer Error in X-ray Diagnosis of Rheumatoid Arthritis*

		Second Observer				
		Normal or Doubtful	Slight	Moderate	Marked	Total
		Hands				
First Observer	Normal or doubtful	8 (1)	4 (3)	—	—	12
	Slight ..	1 (1)	3 (3)	1 (1)	—	5
	Moderate	—	—	1 (1)	—	1
	Marked..	—	—	—	1 (1)	1
	Total	9	7	2	1	19
		Feet				
First Observer	Normal or doubtful	12 (4)	1 (1)	—	—	13
	Slight ..	—	—	—	—	—
	Moderate	—	—	5 (5)	—	5
	Marked..	—	—	—	1 (1)	1
	Total	12	1	5	1	19

The numbers in parentheses indicate proved cases of rheumatoid arthritis.

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BLOOD SUPPLY OF THE FEMORAL HEAD

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[WITH SPECIAL PLATE]

Towards the close of the eighteenth century William Hunter had raised London to the position of one of the best anatomy schools in Europe. He visited Albinus, the celebrated Dutch anatomist, in 1748, and admired his injected anatomical specimens. On returning to London, Hunter developed and elaborated this technique, and many of his original examples are preserved in the Hunterian Museum at the University of Glasgow. This collection contains a number of illustrations of the circulus articuli vasculosus, which Hunter had described originally in 1743.

Materials and Methods

The injected specimens used in this investigation were removed from recent post-mortem bodies or from the anatomical dissecting-rooms. They were dehydrated and cleared in oil of wintergreen (methyl salicylate). Red lead and starch were employed for the intra-arterial injections in Figs. 1 and 2 and indian ink was used for Figs. 6 and 7.

Circulus Articuli Vasculosus.—Since Hunter's original description, this vascular articular anastomosis has been given various anatomical situations. In his account Hunter states, "All round the neck of the bone there is a great number of Arteries and Veins, which ramify into smaller Branches and communicate with one another by frequent Anastomoses like those of the mesentery." These vessels he placed by the margins of the articular cartilages in the subsynovial tissues (Figs. 1 and 2). Some more recent accounts put the circulus articuli vasculosus at the attachment of the joint capsule to the bone. This attachment may coincide approximately with the margin of the articular cartilage in those diarthrodial joints which permit little movements, such as the joints between the intervertebral articular facets. In the adult femoral neck, however, the regions are separated by from 2 to 5 cm. The head of the femur derives its main blood supply from the subcapital anastomosis, as the contribution via the ligamentum teres is, at any age, limited to a small medial segment of the head of the femur. Davies (1946), when discussing the dynamics of haemarthrosis, emphasized the richness and superficial position of the capillary fringe in the synovial membrane.

Retinacula.—The arterial circle at the base of the femoral head is supplied by arteries situated on the neck of the femur between the synovial membrane and periosteum. The vessels are concentrated postero-inferiorly, superiorly, and occasionally anteriorly. The synovial membrane covering these vascular bundles is thrown into longitudinal ridges, to which the term "retinacula" was first applied by Weitbrecht, of St. Petersburg, in 1742. The postero-inferior retinaculum is a very definite structure in the human femur, and shows as a duplication of synovial membrane measuring 1 cm. or more in 76% of specimens examined (Figs. 2, 3, and 4). This pleat of synovial membrane always contains medium-sized arteries, situated at the attachment to the periosteum of the neck or anywhere along the pedunculated area (Figs. 2, 4, and 5).

The Pericapsular Anastomosis.—The afferent arteries to the retinacular vessels are derived from another anastomosis on the capsular attachment towards the base of the neck. This pericapsular corona, which is part of the trochanteric anastomosis, gets its blood supply from the ascending branches of the medial femoral circumflex, the superior gluteal, the obturator, and profunda femoris arteries, as well as from small communications from the acetabular marginal

vessels. Arteries leaving this pericapsular anastomosis enter numerous bony foramina at the base of the femoral neck and pierce small openings in the attachment of the joint capsule. All these arteries are accompanied by a rich plexus of veins, which play an important part in the intravascular thrombosis associated with avascular necrosis of the femoral head.

Ontogeny

During the growth period the circulus articuli vasculosus is situated on the periphery of the epiphysial plate of cartilage and sends branches deeply to the bony epiphysis as well as recurrent vessels to the actively growing metaphysial region (Fig. 6). The marked vascularity of this juxta-epiphysial area, compared with the adjacent diaphysial bone, is obvious in injected specimens (Fig. 7). Harris (1933) pointed out that these metaphysial vessels terminate in large tortuous loops as end-arteries—in contrast to the epiphysial vessels, which anastomose freely. The retinacula in the growing child are well developed, but they are shorter and more firmly attached to the periosteum of the neck than in the adult hip-joint.

Freshly injected specimens demonstrate that the greatest concentration of intra-osseous blood vessels is in the region of Babcock's triangle. This triangle appears in antero-posterior skiagrams as an area sparse in trabecular bone situated inferiorly to the femoral head. An equally obvious triangle, often obscured by the acetabular rim, is seen superiorly at the junction of head and neck (Fig. 8). In fact, the whole base of the head is surrounded by this triangular tunnel, which is utilized by blood vessels to supply and drain the head of the femur. The afferent arteries to this vascular circle can be seen entering the subcapital bony foramina (Fig. 2).

Conclusions

The head and neck of the femur derive their significant blood supply from the pericapsular anastomosis at the base of the neck. The vessels which pierce the capsular attachment are subject to severe trauma and compression in dislocations of the hip-joint and in basal fractures of the femoral neck. These factors, together with pressure from local haemorrhage, jeopardize the vascular channels of the head of the bone.

Basal fractures of the neck of the femur in childhood are frequently complicated by avascular necrosis of the head. The more firm attachment of the synovial membrane to the periosteum of the neck is suggested as an aetiological component for this complication. While the epiphysial plate of cartilage is present the head of the femur depends on the retinacular vessels for its nutrition, as the consensus of reliable opinion is that the vessels in the ligamentum teres are immaterial for the vitality of the head.

Babcock's triangle is a common site for the early manifestations of bony tuberculosis of the hip-joint in children. This very vascular growing region, which is subject to repeated minor traumata and has a slow rate of blood flow, offers a well-protected culture bed for any circulating tubercle bacilli.

In transvesical adduction fractures of the femoral neck the superior and anterior retinacular vessels are always torn, whereas the vessels in the pedunculated postero-inferior retinaculum often escape actual rupture in their continuity but are badly distorted. This alteration of alignment and lumen, which slows or obstructs the local circulation and may lead to eventual thrombosis and avascular necrosis, is a strong argument in favour of early and gentle reduction of this fracture as advocated by recent writers.

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HYPOTHERMIA WITH AUTONOMIC BLOCK IN MAN

BY

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The reduction of oxygen consumption that accompanies a fall in body temperature and the possibilities that induced hypothermia opens up in the field of cardiac surgery and for the poor-risk patient have been the topics of numerous recent publications (Bigelow, Callaghan, and Hopps, 1950; Bigelow, Lindsay, Harrison, Gordon, and Greenwood, 1950; Churchill-Davidson *et al.*, 1953; Annotation, *Brit. J. Anaesth.*, 1953; *Lancet*, 1953). So obvious are the advantages of a state of affairs wherein the cellular oxygen requirements are markedly reduced that they need not be further discussed.

In the past local hypothermia had been produced for a variety of purposes—for example, the relief of pain (Bell, 1812) and the treatment of carcinoma (Arnott, 1851)—but it was not until 1936 that Smith and Fay first induced generalized hypothermia as a treatment for neoplasm (Smith and Fay, 1939). These workers appreciated the necessity of abolishing the body's normal reactions to cold—namely, shivering and vasoconstriction—to facilitate the cooling, and for this purpose they used deep narcosis. The increase in oxygen consumption produced by shivering had already been noted by Voit in 1878, and it was not until 1916, when Krogh eliminated this reaction by curarization, that a fall in oxygen consumption could be demonstrated at lowered body temperatures (Martin, 1930).

In 1948 McQuiston pointed out the possibility of applying the principle to cardiac surgery in hypoxaemic children, and published details of 25 cases (McQuiston, 1949).

The term "artificial hibernation" was originally used by Simpson (Simpson and Herring, 1905) and later by Smith and Fay (1939) to describe the state of induced generalized hypothermia. The recent reintroduction of the term is due in the main to the French workers Laborit and Huguenard (1951). They first studied the potentiation of anaesthesia by promethazine ("phenergan") and diethazine ("diparcol") (Laborit, 1950), and postulated that these drugs produced a partial block of the autonomic nervous system, thus diminishing the body's unfavourable reactions

to surgical trauma (Goldblat, 1951). These workers believe that in certain circumstances death may result from overaction of the autonomic nervous system in an attempt to maintain constant the body's internal environment (Laborit and Huguenard, 1951). Following this reasoning, they attempt to produce a block as complete as possible of the neurovegetative system at all levels, and it is this state which they refer to as "artificial hibernation." To achieve this result the "lytic cocktail" was devised, consisting of the above-mentioned drugs, together with pethidine and chlorpromazine ("largactil"). This latter is known to be a profound depressor of autonomic activity (Courvoisier *et al.*, 1953). A mild degree of hypothermia (34–35° C.) is used to reinforce the autonomic block (Huguenard, 1953).

The technique which we describe is a combination of induced hypothermia and "artificial hibernation," wherein the lowered body temperature is obtained by surface cooling, the lytic cocktail being employed to eliminate the body's normal responses to cold. Our object differs from that of the French workers in that we are primarily concerned with obtaining a reduction in body metabolism, the autonomic block being used only to facilitate the production of hypothermia.

The studies of Kayser and Hiebel (1952) have shown how inaccurate is the term artificial hibernation as applied to man. For this reason we prefer to call the technique "induced hypothermia with autonomic block." This paper is a report of 26 cases in which this technique has been used for major surgery.

Techniques

Production of Autonomic Block and Cooling

With a few minor exceptions the technique followed was the same in all cases. Premedication consisting of pethidine, 100 mg., and promethazine was given intramuscularly three to four hours pre-operatively. An intravenous infusion of normal saline or 5% dextrose was set up about one hour later as a vehicle for administration of the lytic cocktail. The constituents of this were the same for all cases—namely, chlorpromazine 50 mg. (2 ml.), pethidine 100 mg. (2 ml.), and promethazine 50 mg. (2 ml.). Because of the irritant effect of chlorpromazine the injection was made into the drip tubing as far away from the needle as possible. The initial injection was generally 2 ml., followed by supplements of 0.5 to 1 ml. at intervals of 15 to 20 minutes. Modifications in this dosage are discussed later.

Those patients who were not asleep before the beginning of the infusion became unconscious after the first or second dose of the cocktail. With one exception this had occurred within 30 minutes of administration of the first dose. The rapidity of onset of unconsciousness and its depth were a guide to the time to begin surface cooling. On an average this was one and a half hours before operation (range one to three hours). Ice-bags were first placed on the groin, and, in the absence of a response to this, the body was completely covered with ice. Shivering was looked for closely, and its occurrence taken as an indication for a further dose of the cocktail. In all cases cooling was continued until the patient was taken to the theatre. The amount of ice used in the early cases was much less than in later ones; this was partly due to attempts to follow the French methods and partly to caution with a new technique.

During the period of preparation, observations were made of B.P., pulse, and respiration every 15 minutes. Rectal temperatures were taken with a thermocouple which had been previously checked against a mercury clinical thermometer. These were recorded together with frequent observations on the condition of the patient, as assessed by colour, degree of consciousness, presence or absence of shivering, and the drugs administered.

Anaesthesia

The principles of this did not vary from those we would have used for similar cases under normal circumstances. Abdominal and thoracic cases received a sleep dose of barbiturate (if necessary), a relaxant, and nitrous oxide and oxygen (usually 2 litres of each), respiration being controlled or aided throughout. Endotracheal intubation by the oral route was carried out in every case. Induction in non-abdominal cases was with thiopentone and suxamethonium, intubation following topical application of 2% amethocaine or lignocaine to the larynx. Maintenance was with nitrous oxide and oxygen, with or without trichlorethylene or pethidine. There was an enormous variation in dosage from that which would be expected in normal cases, and this is discussed later. Replacement of blood loss was carried out as for normal cases. During the operation observations were made as for the period of cooling.

Rewarming

No attempts were made to hasten this process. On return to bed the patients were covered with a single sheet, and the appearance of shivering was an indication for the application of further covering. It was explained to the nursing staff that for the first 12 hours or so after operation they were to consider their patients to be poikilothermic and to treat them as such, removing blankets should a hyperpyrexia occur. In addition to the routine observations of temperature, B.P., etc., details were noted of post-operative analgesics and sedatives as regards both dosage and time of administration. Note was made of when the patients responded to their name, and this was later compared with the time when they themselves thought they wakened.

Special Investigations

Oxygen uptake was determined at various times during the cooling, the operation, or the rewarming in 12 cases, all of which maintained their spontaneous respiration comparatively undepressed. This was determined by using a Benedict–Roth spirometer. Pre-operative readings were carried out before the pethidine and promethazine were given. Observations during operation were limited to those cases in which, because of the depth of unconsciousness produced by the lytic cocktail and hypothermia, it was possible to avoid the use of an inhalational anaesthetic agent. It was felt that the presence of a gas such as nitrous oxide would unduly complicate the interpretation of results. Towards the end of the series routine analysis of the urine was carried out before and for several days after operation.

Observations

Table I gives a list of operations performed and details of patients.

TABLE I.—*Details of Patients and Operations*

Case No.	Sex	Age	Operation	Duration Hr.	Min.
1	M	24	Portocaval anastomosis	4	40
2	M	33	Oesophago-jejunostomy	4	20
3	M	25	Devascularization of stomach and oesophagus	4	25
4	M	61	Total cystectomy	4	30
5	F	50	Pyelolithotomy	1	20
6	F	44	Partial gastrectomy	2	30
7	F	64	Radical mastectomy	2	0
8	M	60	Partial gastrectomy	2	20
9	F	24	Thyroidectomy	1	5
10	F	58	Splenectomy	2	5
11	M	55	Oesophago-jejunostomy	5	20
12	F	59	For intestinal obstruction		45
13	F	24	Exploration of femur	1	0
14	M	52	Colectomy	2	5
15	M	57	Devascularization of stomach and oesophagus	2	45
16	M	77	Bladder diverticulectomy	2	30
17	F	48	Mitral valvotomy		45
18	F	20	Thyroidectomy	1	0
19	F	60	Oesophago-gastrectomy	3	35
20	M	53	Laparotomy-colostomy		35
21	F	47	Oesophago-gastrectomy	4	10
22	M	53	Devascularization of oesophagus and gastrectomy	6	25
23	M	57	Splenectomy		35
24	F	73	Total cystectomy	4	0
25	F	60	Exploration of bile ducts	1	30
26	F	47	Total cystectomy	3	30

Respiratory System

Despite the fact that neither atropine nor hyoscine was given as premedication, no increase in secretions was noted during either cooling or operation in any case. The lytic cocktail invariably slowed the respiratory rate, but this was accompanied by a slight increase in tidal volume. At the temperatures which we reached before operation (36° to 27.4° C.) there were no instances of alarming decreases in respiratory rate, 8 to 10 a minute being the average when the patients were taken to the theatre. These changes were reversed during rewarming. Diminished sensitivity of the larynx, as might be expected from the doses of pethidine used, was very marked. Intubation was carried out in six cases at the end of the cooling, without any barbiturate, and in no instance was there a very pronounced reaction from the patient. This laryngeal insensibility was a disadvantage in one case.

Case 20.—The operation was laparotomy for intestinal obstruction. During cooling, moist sounds in the chest were heard and pulmonary oedema was diagnosed. On closer examination silent regurgitation of gastric contents was detected. Tracheal suction was carried out and the passage of an oesophageal tube revealed a full stomach.

Cardiovascular System

Average blood-pressure changes during the cooling and the operation are shown in Table II, and the suggested principal factors causing the pressure falls during operation in Table III. Hypotension of varying degrees occurred during establishment of the autonomic block in every case and during most of the operations. Pressure falls following the first 2 ml. of the cocktail varied enormously from patient to patient and were unpredictable. This led us to introduce a test dose of 1 ml. in poor-risk cases, subsequent doses depending on the B.P. response to the first injection. The fall in B.P. which followed administration of the lytic cocktail had a large postural element in each case, and could be reduced, but not abolished, by raising the foot of the bed (Fig. 1). The rise in pressure that was noted in one case during operation was attributed to the Trendelenburg position, which was used during the whole procedure.

TABLE II.—*Blood-pressure Changes During Cooling and Operation*

During cooling and autonomic block:	
Fall	26 cases
During operation:	
No change	5 „
Rise	1 case
Fall	20 cases
Actual readings:	
Average fall during cooling	45/30
„ pre-op. B.P.	110/80
„ during operation	80/55
„ fall	30/25
„ minimal B.P. during operation	60/30
„ maximal fall	50/50

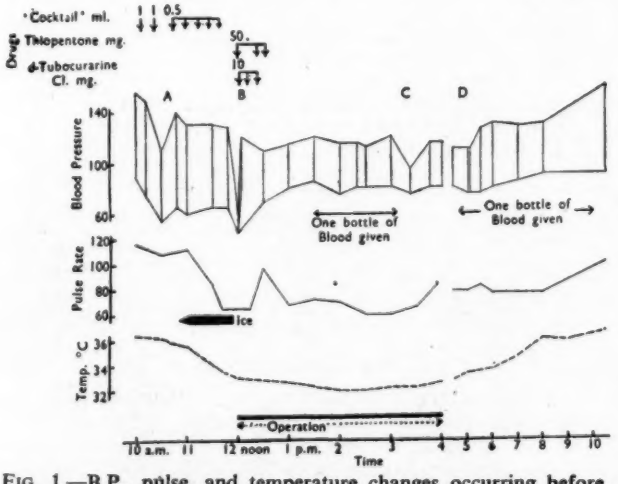

FIG. 1.—B.P., pulse, and temperature changes occurring before, during, and after operation in Case 24. Postural falls in pressure occurred as follows: A=after first dose of cocktail with patient sitting up; B=removal from bed to theatre; C=when head of table was raised. A and B were treated by the head-down position and C recovered spontaneously. D=patient back in bed.

From Table II it can be seen that pulse pressure is affected little during the operation, even at the lowest pressures. This might be expected because of vasodilatation due to chlorpromazine. A prominent feature throughout the series was the extreme sensitivity of the B.P. to haemorrhage. Quite significant falls occurred after even slight loss, the pulse remaining almost unchanged. This is due to loss of compensatory mechanisms.

TABLE III.—*Suggested Principal Factors Causing Fall of B.P. During Operation*

Posture	11	Hypothermia	2
Blood loss	5	Barbiturates	1

In the absence of shivering the pulse rate fell by 10 to 20 beats a minute during the establishment of the autonomic block and cooling. Shivering invariably raised the rate by 20 to 40 a minute. The changes were very variable during operation, but on the whole there was little variation from that produced by the cooling. The average rate during operation was 80 a minute, values ranging from 55 to 104.

Cardiac irregularities were detected in three cases during cooling. In two instances auricular extrasystoles appeared at the lower temperatures, but disappeared spontaneously during the rewarming. These irregularities were of less importance than the auricular and ventricular fibrillation occurring in the following two cases.

Case 21.—A marked fall in B.P. followed the test dose of cocktail. Cooling was easily achieved, the temperature dropping rapidly to 32° C. At this stage cardiac irregularities were detected. Following thoracotomy the temperature fell to 28° C. and the pulse was grossly irregular, remaining so throughout the operation. A post-operative E.C.G. confirmed the presence of auricular fibrillation. Recovery was slow, and 34 hours post-operatively, when the temperature had reached 32.5° C., normal sinus rhythm reappeared.

Case 17.—A woman aged 48 was admitted for mitral valvotomy. She had a grade 3+ condition of her valve and was frequently in failure. She was orthopnoeic, cyanosed, and had a greatly enlarged right ventricle with signs of basal congestion. She was considered an extremely grave risk by the physicians, but, in view of her complete invalidism and hopeless prognosis, exploration was thought to be justified. After 4 ml. of cocktail the temperature dropped to 32.5° C. Her condition was described as much improved and she had become pink in colour. Her B.P. had dropped from 110/60 to 80/50 and her pulse rate from 80 to 48. When her temperature had reached 31.8° C. ice-bags were applied, and an hour later the temperature was 30.7° C. but her B.P. suddenly became unrecordable. Her pulse rate was 60. Elevation of the foot of the bed restored the B.P. to 85 systolic. Unfortunately, there was a delay in beginning the operation owing to the previous case taking much longer than had been estimated, and her temperature was allowed to fall to 28.4° C. before she was taken to theatre. This was 4 hours 20 minutes after the initial dose of cocktail and three hours after the first application of ice. Her systolic B.P. was 95 and she had had 9 ml. of cocktail. Her pulse was satisfactory, and she was pink. On opening the chest her temperature fell nearly 3°, to 25.7° C., and her heart rate slowed to 50. The surgeon estimated her systolic pressure at 100 and her pulmonary arterial pressure at 60 mm. Hg. The heart seemed to have shrunk to less than its normal size and did not fill the pericardial sac. The ventricular beat seemed weak and rather ineffective. On dilatation of the valve ventricular fibrillation began and was arrested after five and a half minutes by application of an electrical defibrillator (110 V. in 0.1-second impulses). Normal beat was resumed, but fibrillation recurred during suture of the auricular appendage. All efforts to restore this heart failed.

In the majority of cases the B.P. and pulse returned to normal as the temperature rose. In a few patients, however, a secondary fall in B.P. occurred about one to two hours post-operatively This always responded to posture and small transfusions.

Temperature Changes

On the average a drop of 0.5° C. was obtained during the administration of the cocktail before the application of ice. During the period of cooling before operation a further average drop of 3.4° C. (1 to 10° C.) occurred. Fig. 2 shows temperatures existing during operation in 24 cases. Perhaps the most significant observation was the fall in temperature of about 2° C. occurring in all cases in which the chest was opened. This did not take place after abdominal section.

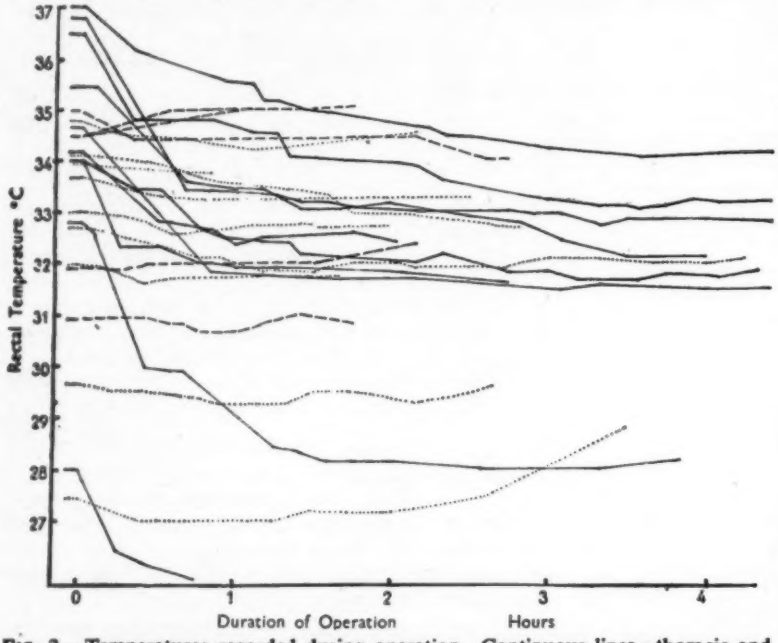

FIG. 2.—Temperatures recorded during operation. Continuous lines = thoracic and abdomino-thoracic cases. Dotted lines = abdominal cases. Broken lines = non-abdominal cases.

The majority of patients had regained their normal temperatures in about 10 hours after operation, though one case already reported (Case 21) remained subnormal for 48 hours.

Bleeding

This varied considerably from case to case, and apparently bore little relation to the existing B.P. In 14 cases there was a marked postural ischaemia; in four cases, despite suitable posturing, bleeding was much increased, while in the remaining eight the amount of bleeding appeared normal. One case of reactionary haemorrhage occurred. This took place 16 hours post-operatively and was of moderate severity.

Excessive bleeding in the absence of any rise in arterial B.P. may be attributable to a rise in venous pressure. This may be a factor at lowered temperatures, when, as has been shown by Bigelow, Lindsay, and Greenwood (1950), venous pressure is likely to rise.

Case 7.—This patient showed excessive bleeding during radical mastectomy; the degree of hypothermia was only moderate (34° C.), but may have been sufficient to exacerbate an already raised venous pressure due to a failing myocardium.

Apart from any consideration of the B.P., bleeding at low temperatures may be due to some interference either with the ability of vessels to retract or with the formation and contraction of blood clot. This may have applied to Case 22.

Case 22.—This man, undergoing splenectomy and transection of the stomach for portal hypertension, bled excessively throughout the operation, which, largely for this reason, lasted six and a half hours. During most of the time his B.P. ranged from 50 to 90 systolic and 40 to 65 diastolic. All efforts to arrest the oozing in the portal bed were unsuccessful, and when the patient was returned to bed his rectal temperature was 31.5° C. and blood was pouring out of his under-water drain almost as fast as it was transfused. Owing to the large replacement of blood, adequate amounts of calcium gluconate and vitamins C and K were added to the transfusions, but only when the temperature reached 32° C. did the haemorrhage stop. At this time he had received 19 pints (10.8 litres) of blood; the measured loss corresponded. Altogether during and following his operation this man received a total of 21 pints (11.9 litres) to compensate for his loss, and he died 48 hours later, apparently from a transfusion reaction. Necropsy was not performed. At operation the liver was about half the normal size and an advanced degree of cirrhosis was present. The pathologist expressed the opinion that it was remarkable how he had managed to carry on with so little liver tissue. There seemed little doubt that this man's prothrombin level was so low that the clotting of his blood even with slight degrees of hypothermia was seriously affected.

Anaesthesia

The total dosage of all drugs given in thoracic and abdominal cases is shown in Table IV. From this it is immediately apparent that there is a striking reduction in the amount of thiopentone used. If those cases with liver damage are excluded a similar, though less marked, reduction in the amount of D-tubocurarine chloride used is evident. In cases with liver damage comparatively large doses of D-tubocurarine chloride were required (Table V), showing that the observation of Dundee and Gray (1953) in this respect holds true in hypothermic patients. Reversal of the effects of the D-tubocurarine chloride by neostigmine at the end of operation was as in normal cases (Fig. 3). Where suxamethonium was used for intubation its duration of action was normal.

TABLE IV.—*Total Dosage of Anaesthetic Agents in 22 Abdominal and Thoracic Cases*

Thiopentone	No. of Cases	D-tubocurarine Chloride	No. of Cases*
Nil	7	Up to 20 mg.	6
Up to 100 mg.	7	20–30 mg.	5
100–200 mg.	4	30–40 mg.	4
250 mg. +	4	40 mg. +	1
Pethidine	**No. of Cases**	**Others**	**No. of Cases**
Nil	18	Nil	15
Up to 50 mg.	3	Lytic cocktail	5
50 mg. +	1	Chlorpromazine	2

* Excluding five cases with known liver damage. One case received gallamine triethiodide as relaxant.

TABLE V.—*Comparison of Amount of D-tubocurarine Chloride Required by Patients with Abnormal Liver Function, and Those in Whom There Was no Reason to Suspect Liver Damage*

Liver Function	No. of Cases	Average Duration of Operation (Minutes)	Average Dose of D-tubocurarine Chloride (mg.)
Normal	16	160 (35–320)	26 (5–48)
Abnormal	5	244 (145–385)	58 (50–75)

Post-operative Period

One formed the impression that the general condition of these cases was better than normal after operation. There was a reduction in the amounts of analgesics needed in the first two post-operative days, compared with normal requirements (Table VI). Seven subjects received no sedative or analgesic drug from the end of operation to their discharge from hospital. Although, on the average, patients responded to their names about three and a half hours after opera-

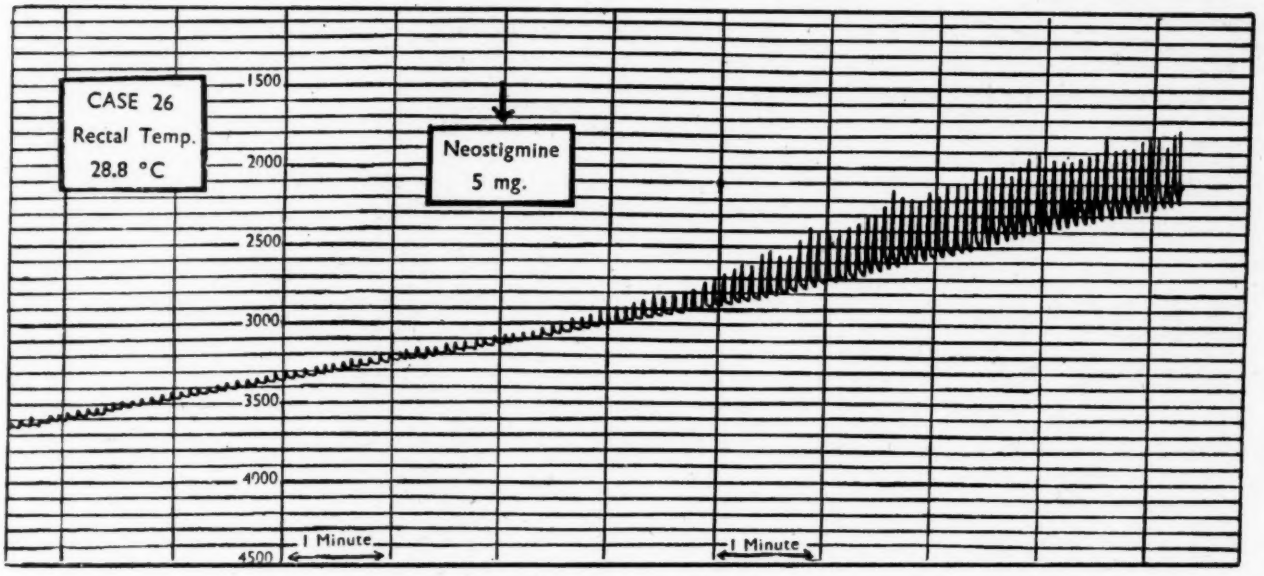

FIG. 3.—Spirometry tracing showing satisfactory reversal of gallamine triethiodide by neostigmine. The last dose of relaxant (40 mg.) had been given 30 minutes before the neostigmine.

tion, yet they themselves think that they did not waken for a further seven hours. This time is significant, as it coincides with the time of administration of the first dose of analgesic.

The complications occurring during this period are listed in Table VII. The three cases with respiratory trouble cleared up with orthodox treatment. The haematemesis which occurred in Case 24 was attributed to trauma during removal of the thermocouple from the oesophagus. It is worth mentioning that this was the only occasion on which rectal temperatures were not recorded, the reason being that excision of the rectum was contemplated in addition to removal of the bladder. Paralytic ileus, which eventually proved fatal in Case 4, was attributable to the surgical procedure, although one cannot dismiss the possibility that autonomic block played some part.

The only hyperpyrexia that was noted occurred in our first case, which is worthy of mention.

Case 1.—The patient was returned from the theatre with a temperature of 34° C. and instructions were given that readings should be taken every 15 minutes. Two hours later a nurse, who was not conversant with the thermocouple, took the oral temperature and found that it was not recordable by a clinical thermometer. She immediately covered the patient with a heat cradle, and by the time the next reading was due the temperature was 39° C. Once the source of heat was removed the temperature gradually returned to normal.

Nursing staff who have been trained to conserve body heat on all occasions find it difficult to get used to patients lying in bed after operation covered only by a sheet. When the lessons from this case were pointed out to them we had no more trouble.

TABLE VI.—*Post-operative Analgesics (22 Cases). All Analgesics Recorded as Equipotent Doses of Pethidine (10 mg. Morphine or 8 mg. Methadone Considered Equal to 100 mg. Pethidine)*

A. Average dosage and time of administration of first dose from end of operation, compared with average requirements of 27 unselected cases, having orthodox anaesthesia and undergoing similar operations

	First Dose		Total Dosage (mg.)	
	Time from End of Operation	mg.	First 24 Hrs.	Second 24 Hrs.
Hypothermia	10·5 hrs.	60	100	140
Orthodox anaesthesia ..	3·25 „	130	340	250

B. Analysis of dosage in cases of hypothermia

	No. of Cases	
	First 24 Hours	Second 24 Hours
Pethidine:		
Nil	7	7
100 mg.	12	6
200 „	1	6
300+ „	3	4
Promethazine 50 mg. ..	3	1
Phenobarbitone 200 mg.	1	1

TABLE VII.—*Post-operative Complications (Excluding Ketosis, as This was not Looked for in Every Case)*

	No. of Cases
First 48 hours:	
Vomiting	3
Restlessness	3
Lobar collapse	2
Pneumonia	1
Continued haemorrhage	1
Reactionary „	1
Prolonged hypotension	1
Sudden B.P. fall	1
Paralytic ileus	1
Haematemesis	1
Hyperpyrexia	1
Later:	
Paralytic ileus	1
Pulmonary embolism	1

Deaths

Five deaths occurred in this series of cases (Table VIII). We feel that in two cases (Cases 17 and 22) hypothermia may have contributed to the outcome. One cannot dismiss the possibility that the technique played some part in Cases 4 and 24, although this seems unlikely, since the deaths occurred on the 16th and 13th post-operative days respectively. It is difficult to say what parts surgery and hypothermia played in the following case.

TABLE VIII.—*Cause of Death*

Case No.	Time Post-operatively	Cause
4	16 days	Paralytic ileus and peritonitis
16	24 hours	Peritonitis and cardiac failure
17	On table	Ventricular fibrillation followed by asystole
22	48 hours	? Transfusion reaction
24	13 days	Pulmonary embolus

Case 16.—This patient suffered from senile dementia with incipient cardiac failure. The instability of this cardiovascular system was shown by a marked B.P. fall following the first dose of cocktail. Hypotension persisted throughout the cooling and for most of the operation, during which the temperature fell to 31.6° C., at which the pulse became irregular. There was a moderate reactionary haemorrhage 16 hours after operation. Rewarming was slow, but the patient's condition gradually improved.

Death occurred suddenly 24 hours post-operatively, when the temperature had reached 34° C. Necropsy revealed peritonitis and appearances suggestive of left ventricular failure.

Difficulties Encountered During Production of Autonomic Block and Hypothermia

In 17 cases there was no shivering or difficulties of any kind. Since this is a new technique the difficulties we encountered in the remaining nine cases are discussed in detail. These are listed in Table IX. Inability to control shivering

TABLE IX.—*Difficulties During Cooling*

	No. of Cases
Shivering difficult to control	4
Difficulty in producing hypothermia	3
Cardiac irregularities	3
Regurgitation	1
Restlessness	1
Uncontrollable B.P. fall	1

was generally accompanied by a slow fall in temperature. Resistance to the production of autonomic block occurred in the following four cases.

Cases 9 and 18.—Whereas the average dose of cocktail was 7 ml., in the presence of thyrotoxicosis we administered 12 and 13 ml. respectively to these patients, supplemented by intramuscular pethidine and diethazine in No. 18, and with thiopentone in both. Once the initial difficulties were surmounted, satisfactory cooling occurred in both.

Case 13.—This patient was a morphine addict, and even after 10 ml. of the cocktail the autonomic block was incomplete, and the rectal temperature never fell below 35.5° C.

Case 23.—Although this patient weighed only 9 st. 7 lb. (60 kg.) and had a Hb of 41% he proved the most difficult case encountered to date. The administration of 12 ml. of the cocktail over 100 minutes produced no effect on the B.P., and intense shivering was occurring. During the next hour 50 mg. of pethidine and 150 mg. of diethazine were given intramuscularly, the same doses together with 50 mg. of chlorpromazine and 50 mg. of thiopentone being given intravenously. This did not abolish shivering and the temperature fell to only 35° C. Shivering was then controlled by curarization, but in spite of the intensive application of ice the temperature fell by only 1° C. in 50 minutes.

This subject had been receiving nightly doses of butobarbitone (400–600 mg.) and promethazine twice daily for a month. These may have led to a tolerance to the drugs administered, but cannot explain the resistance to cooling when shivering had been completely abolished.

Further difficulties are illustrated in the following cases.

Case 11.—In this instance there was considerable doubt about the activity of the chlorpromazine. Despite the elimination of obvious shivering, presumably accomplished by the pethidine (Dundee *et al.*, 1953), the fall in temperature was negligible. This view is substantiated by the appearance of vasoconstriction following the application of ice.

Case 2.—A peculiar feature here was the almost complete absence of the usual narcotic effects of the cocktail despite a satisfactory response in all other respects. This deficiency was remedied by the use of 25-mg. doses of thiopentone.

Special Investigations

Oxygen Intake.—Fig. 4 includes all the observations that were made on 12 subjects, values being expressed as a reduction from the normal and temperatures as falls from 37° C. As can be seen, it was possible to follow only half the patients throughout the whole procedure, but isolated observations on the remainder were in agreement with these. The overall picture of falls in oxygen intake with hypothermia agrees with the findings of Bigelow, Lindsay, Harrison, Gordon, and Greenwood (1950) and Dundee, Scott, and Mesham (1953) in dogs. A constant observation not shown in Fig. 4 was a drop of 8–10% in oxygen intake that occurred after the cocktail, before the application of ice and drop in body temperature.

Urine Analysis.—This was done in eight cases only. A slight reddish coloration was present for three to four days in three cases. There was no haematuria on spectroscopic examination, and the colour is probably due to the breakdown products of the phenthiazine derivatives, as two of these cases received promethazine as a sedative in the post-operative period.

The presence of ketone bodies could be detected in three cases after cooling and post-operatively, although clinically and biochemically there was no evidence of acidosis. In one case this persisted until the fifth post-operative day, but

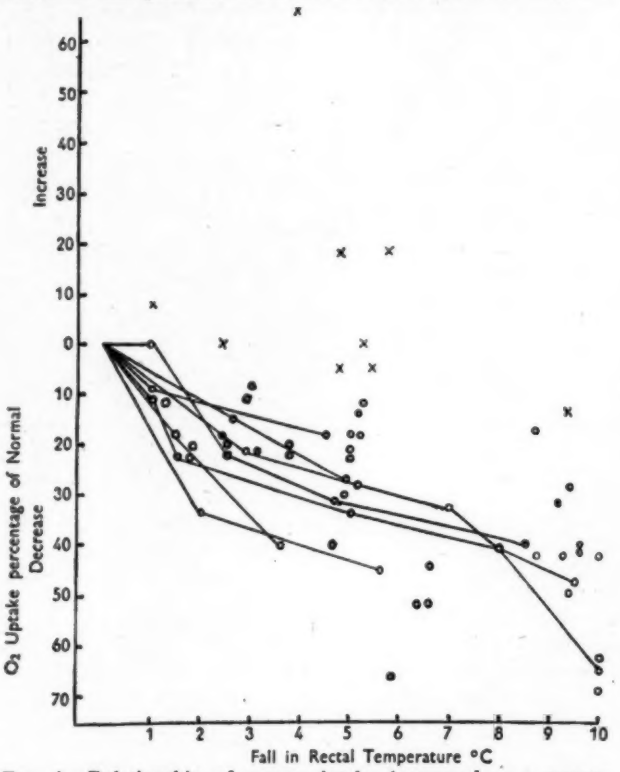

FIG. 4.—Relationship of oxygen intake (expressed as a percentage of normal) to fall in rectal temperature (expressed as variation from 37° C.). o——o = observations made in the absence of shivering. Those joined together are serial readings during cooling and operation. O indicates isolated observations at any period of the procedure. X = readings taken when the patient was shivering.

cleared up after 48 hours in the others. Glycosuria was detected in two cases; in both instances the patient had received dextrose intravenously when the temperature was 30–32° C. This cleared up when the temperature was raised. Depression of the glycogenic activity of the liver at low temperatures is a possible explanation of this phenomenon.

Discussion

This paper has been written with the purpose of drawing attention to some dangers of hypothermic techniques. All the patients in this series stood to benefit from the production of hypothermia. Some who were rejected for anaesthesia by orthodox techniques made a highly successful recovery. The high mortality occurred in the group of patients who were seriously ill and who were grave operative risks by any standards. It is considered that in this group the method gave the best chance of survival. Our purpose in observing this series has been to obtain a preliminary assessment of the method of producing hypothermia by external cooling combined with autonomic block. It is useful to know that reduction of temperature can be satisfactorily and easily produced in patients, without the necessity for an extracorporeal arteriovenous shunt (Delorme, 1952), a procedure which it seems to us carries its own risks. It is apparent from our experience that any degree of hypothermia can be obtained by this technique. It is a method, moreover, which avoids an undesirable depth of anaesthesia or prolonged periods of respiratory arrest due to curarization, which would otherwise be necessary to avoid shivering.

Our experience both in this series and in animal experiments has led us to two conclusions. First, that the danger

of serious cardiac irregularity at temperatures lower than 28° C. is real, and is particularly imminent if cardiac manipulation is required. Secondly, the difference in oxygen consumption between a patient at 28° C. and one at 25° C. is insufficient, in the present state of our knowledge, to warrant the extra risks involved by proceeding to lower temperatures.

The reduction in bleeding during hypothermia has not always been as marked as was expected. At low temperatures the prolongation of the clotting time and/or bleeding time has on occasion been a source of embarrassment. We are proceeding to investigate the effect of different prothrombin levels on the clotting time of blood at different temperatures. We feel that, before hypothermia is employed for cases of portal hypertension with liver cirrhosis, the clotting-time of the patient's plasma should be estimated at various temperatures so that the critical level may be ascertained.

It seems to us reasonable also that hypothermia might be an added risk in patients whose myocardium is damaged (see Cases 7, 17, and 21). Initial heart–lung experiments which we have performed in the dog have confirmed the findings of Knowlton and Starling (1912) that the myocardium is affected at lower temperatures, and suggest that the Starling response to stretching the myocardial fibres is less efficient. It is therefore questionable whether any degree of hypothermia—say below 30° C.—is justifiable in cases with a damaged myocardium until further work has been carried out to elucidate this problem.

A weakness in this technique has been the comparative lack of control of the patient's temperature. If the hypothermia becomes too intense, as when allowance has not been made for the 2–3° C. fall which always occurs on opening the chest, there is no adequate means of correcting the situation. This is no fault of the autonomic blockade, but is a technical problem, to which we are giving consideration.

The indications for hypothermia would seem to be:

1. When a degree of hypotension is required to control haemorrhage either for patients in whom large blood loss is expected, or in whom even a small blood loss will embarrass the work of the surgeon. We have never been convinced of the safety of hypotensive techniques in which the supply of blood carrying oxygen to the tissues is reduced without any effort being made to reduce to some extent the oxygen demands.

2. In patients with a severe degree of anaemia which cannot be corrected before operation. This series has included four cases of oesophageal varices in which there was a marked degree of anaemia and which responded to transfusion only by further haematemesis. The combination of anaemia with the hypotension which is so helpful to the surgeon in these cases is justifiable only if the oxygen demands of the patient are reduced by hypothermia. This is well illustrated by Case 3 (Fig. 5), when a patient whose Hb was only 50% was maintained for 4½ hours at a B.P. averaging 60/30 (minimum 35/25). His recovery was complete and uneventful.

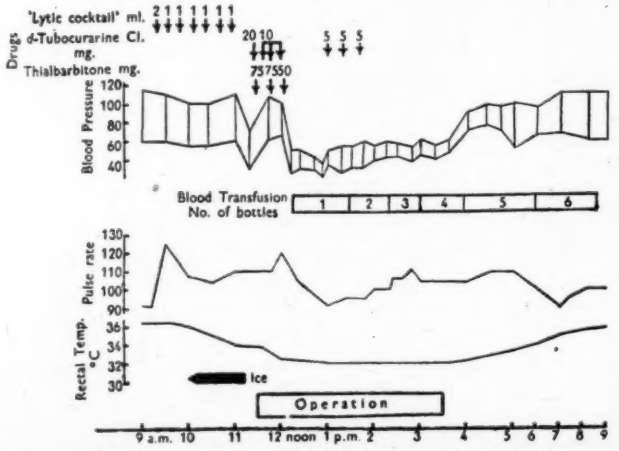

FIG. 5.—B.P., pulse rate, and temperature recordings in Case 3, showing the degree of hypotension that was present for most of the operation.

3. In operations on the heart and great vessels in which it may be necessary to cut off the cerebral circulation for a period of time. In this regard a startling observation was made in Case 17. For 17 minutes, at 25° C., after all possibility of cerebral circulation had ceased, this patient's respiratory centre continued to function, as evidenced by quite normal respiratory movements.

4. In thyrotoxicosis which cannot be controlled by medical treatment. One case in this series had been presented for operation on two previous occasions and returned to the ward because of an uncontrollable pulse rate of 160 a minute. Induction of hypothermia reduced this to 80 a minute, considerably improved the general condition of the patient, and enabled an operation to be performed, which was followed by an uneventful recovery.

5. Presumably in neurosurgery there will be indications for this technique, but up to the present we have had no experience with this application.

6. In certain therapeutic indications such as hyperpyrexia occurring in pituitary disorders or post-operatively in children, and in thyroid crises.

Summary

The history of the production of hypothermia in man is reviewed, and a method described for its production in man with the help of block of the autonomic nervous system.

The use of this technique in 26 cases undergoing operation is described.

Observations are recorded of the changes that occurred in the respiratory system, the cardiovascular system, and the body temperature, with the amount of bleeding.

Dosages of anaesthetic agents and post-operative analgesics are discussed, as are post-operative complications and deaths that occurred.

The troubles that we encountered during the production of the autonomic block and cooling have received special mention.

Our findings concerning the relationship of oxygen intake to temperature, and the presence of abnormal constituents in the urine following this technique are reported.

We are indebted, among others, to Professor C. A. Wells and Mr. R. W. Doyle, with whose co-operation this study was made possible. We are also grateful to Dr. J. Harper, of Pharmaceutical Specialities (May & Baker) Ltd., for supplying the chlorpromazine (largactil), promethazine (phenergan), and diethazine (diparcol) for this investigation; and also for his courtesy and assistance.

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THE PRODUCTION OF HYPOTHERMIA

BY

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The effect of hypothermia in diminishing the body's oxygen consumption has led to a recent interest in this as an aid to anaesthesia in the poor-risk case and in major surgery. Man is equipped with a highly effective mechanism for combating the effects of cold, and the first step in the production of hypothermia must be to overcome this response. This can be achieved by deep anaesthesia (Bigelow *et al.*, 1950), the use of muscle relaxants (Krogh, 1916), or by the "lytic cocktail" or "liberation cocktail" introduced by the French workers Laborit and Huguenard (Huguenard, 1953).

We have compared the efficacy of these three methods in facilitating the production of hypothermia in the anaesthetized dog by means strictly comparable to those applied in man, and the individual constituents of the "lytic cocktail" have been studied. Their effect on the rate of fall of the rectal temperature after the application of ice, and on the amount of shivering produced, has been studied. We have also investigated the effect of hypothermia, induced with the aid of the constituents of the "lytic cocktail," on oxygen intake, heart rate, and respiration.

Methods

Unselected mongrel dogs were used, varying in weight (8–16 kg.) and age. Basal narcosis was induced by the intraperitoneal injection of 30 mg./kg. pentobarbitone in a 3% solution at approximately blood heat (Adams, 1944). Once the dogs were asleep endotracheal intubation with a cuffed tube was carried out by the aid of a topical application of 2% amethocaine or 2% lignocaine. Forty-five minutes after induction of anaesthesia adjuvant drugs were administered in doses as follows: pentobarbitone, 15 mg./kg.; D-tubocurarine chloride, 3 mg./kg.; chlorpromazine, 2 mg./kg.; pethidine, 4 mg./kg.; promethazine, 2 mg./kg. The "lytic cocktail" comprised all of the last three in the doses mentioned. With the exception of pentobarbitone (which was given intraperitoneally), all drugs were given by deep intramuscular injection mixed with 1,000 Benger units of hyaluronidase. Immediately the muscle relaxant was given the cuff of the endotracheal tube was inflated and the animals' respiration mechanically controlled with oxygen for periods of three to four hours. A similar procedure was adopted when respiration failed because of hypothermia. Fifteen minutes after injection of the adjuvants the animals were covered with ice-bags. Cooling continued for 90 minutes, when the animals were gradually heated up by the help of hot-water bottles and a hair-drier.

These doses of the constituents of the "lytic cocktail" are similar to those which are given to man. The total amount of pentobarbitone (45 mg./kg.) administered to those animals who received it as an adjuvant will result in deep anaesthesia (Adams, 1944). In the case of D-tubocurarine chloride, 3 mg./kg. was given, as we found that this will invariably produce apnoea over the period of our investigations, and it can be safely reversed some three to four hours later by neostigmine 5 mg. and atropine 2 mg.

In order to reduce the factor of individual susceptibility of the dogs to the drugs and to cooling, the experiment was planned so that during its course each animal received each of the adjuvants. As will be reported later, three dogs died during this study. In the case of two of these the death occurred when the last adjuvant drug was being investigated, so that the series with these is complete. In the third instance the fatality was with the first drug, and no readings obtained from this dog are included in the results.

Rectal temperatures were noted by a thermocouple every five minutes, and the presence or absence of shivering was noted at similar intervals. The heart rate was recorded every 15 minutes. Oxygen intake was measured by means of a direct recording of respiration on a spirometer containing oxygen. To reduce resistance to respiration all valves were removed from the instrument and a small soda-lime canister was inserted close to the endotracheal tube. Care was taken to see that the circuit was leak-proof, and at temperatures below 30° C. respiration was aided during the period of observation. This ensures full oxygenation of the blood and eliminates respiratory depression as a cause of decreased oxygen intake (Bigelow *et al.*, 1950). Another factor which may well interfere with the readings is the excretion of nitrogen by the dog when breathing from a spirometer containing oxygen. To overcome this a large flow of pure oxygen was administered by a T-piece once the endotracheal tube was in position, and between readings the animal was maintained on pure oxygen.

Results

On all occasions the normal temperature of the animal was taken as that immediately before the administration of the adjuvant drug—that is, three-quarters of an hour after the intraperitoneal administration of the basal narcotic. For

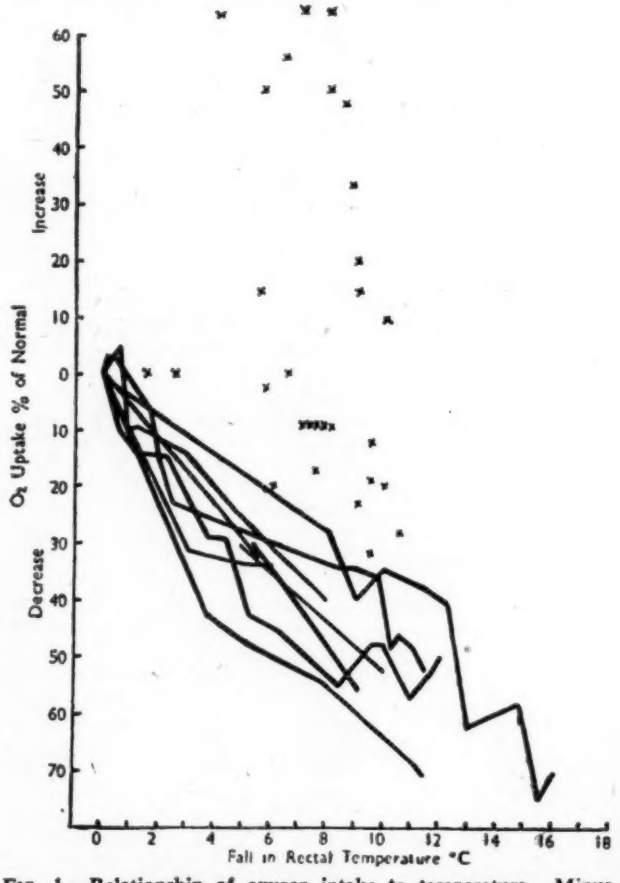

FIG. 1.—Relationship of oxygen intake to temperature. Minus values indicate continuous readings in the absence of shivering. ×, Isolated readings taken when the animal was shivering.

the sake of simplicity all temperatures are recorded as variations from this normal. In order to compare the amount of shivering under various conditions a point system was adopted. The presence or absence of palpable shivering was noted at five-minute intervals, one point being recorded for every positive observation. The average of six observations with each of the drugs studied can be seen in Table I. This shows the fall in temperature which took place every 15 minutes and the total amount of shivering every 30 minutes. In each of these dogs preliminary studies of oxygen intake under the effects of 30 mg./kg. pentobarbitone revealed that there were negligible changes over the period from 40 to 180 minutes after the injection of the barbiturate. Thus any changes which we have recorded are due to the hypothermia or adjuvant drug. As in the case of temperature, the normal readings for oxygen intake, pulse rate, and respiratory rate were taken to be those recorded immediately before the administration of the adjuvant. Changes in oxygen intake are expressed as percentages of the normal, whilst alterations in pulse rate are recorded as absolute changes from normal.

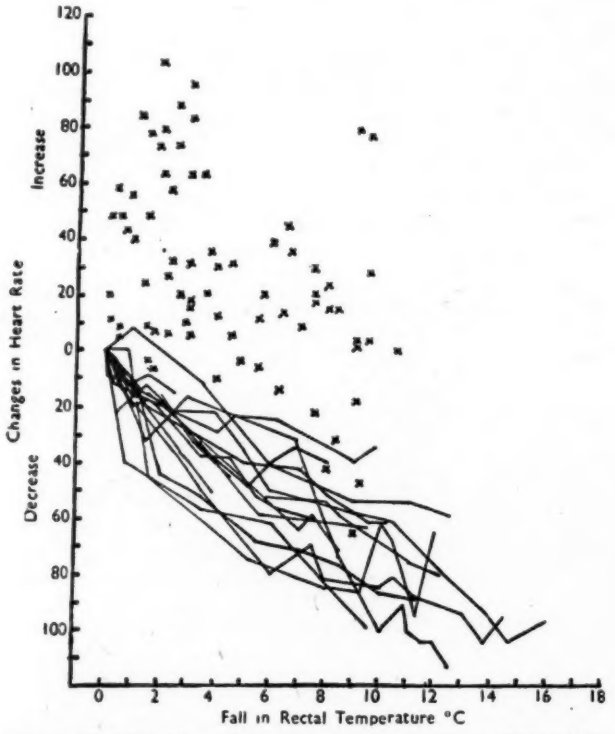

FIG. 2.—Relationship of heart rate to temperature. Minus values recorded when no shivering was occurring. ×, Readings taken during bouts of shivering.

Fig. 1, showing the relationship between oxygen intake and temperature (10 observations), demonstrates a fall in the former as the latter decreases. However, when shivering occurs there is a consistent rise in oxygen demands. The lowered temperature may be seen to have a similar relationship to heart rate and respiratory rate in Figs. 2 (25 observations) and 3 (10 observations) respectively; but here again rises are constantly provoked by the onset of shivering. Apnoea is apt to occur at a rectal temperature of 25° C., but severe respiratory depression has been noted at temperatures of 29° C. and under.

Cardiac arrest occurred in three dogs at temperatures of 23° C., 23.5° C., and 26.5° C., respiration being unaided in all cases. It is significant that lower temperatures (21° C.–22° C.) have been obtained without untoward effects in those animals in which respiration was fully controlled with oxygen.

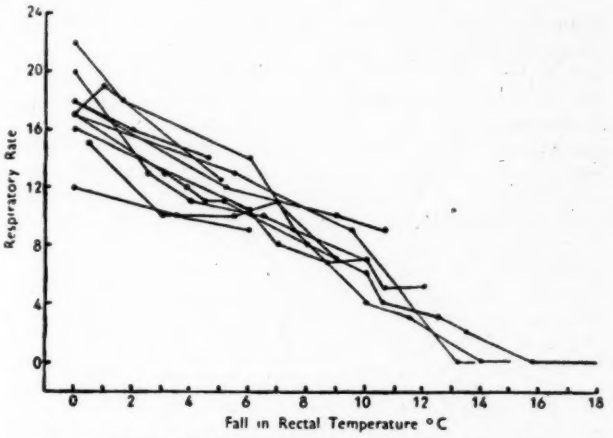

FIG. 3.—Relationship of respiratory rate to temperature.

Discussion

From Table I a comparison of those recognized methods of facilitating the production of hypothermia can now be made. An analysis of the results obtained with deep anaesthesia, curarization, and the "lytic cocktail" is given in Table II. This expresses the average temperature fall obtained using these methods after 90 minutes' cooling as a percentage of that occurring with basal narcosis alone. The amount of shivering which occurred during the last hour of cooling is similarly expressed. It is apparent from Tables I and II that there is little to choose between these three methods as regards rate and amount of temperature fall, and abolition of shivering.

A similar analysis of the effects of the constituent drugs of the "lytic cocktail" is also shown in Table II. From this it may be seen that by far the most active constituent

TABLE I.—*Effects of Various Drugs and Combinations of Drugs on Average Fall in Rectal Temperature in the Dog and Amount of Shivering After Covering with Ice. (See Text for Explanation of Method of Recording Amount of Shivering.)*

Drugs	Dose, mg./kg.	Average Fall in Rectal Temperature °C. Time in Minutes after Covering with Ice						Average Amount of Shivering Time in Minutes After Covering with Ice		
		15	30	45	60	75	90	0–30	35–60	65–90
Pentobarbitone	30	0·8	1·5	2·7	3·7	4·5	5·2	2	4	5·4
Pentobarbitone 30 mg./kg. plus the following, given 45 minutes later:										
Pentobarbitone	15	1·5	3·4	5·1	6·7	7·6	9·1	0	0	0·5
D-tubocurarine chloride	3	1·2	3·2	5·0	6·6	8·1	9·5	0	0·6	0·8
"Lytic cocktail," comprising:										
Chlorpromazine	2	1·7	3·3	5·1	6·9	8·5	10·4	0	0	0·5
Pethidine	4									
Promethazine	2									
Chlorpromazine	2	2·2	3·3	5·6	7·5	9·0	10·6	0	0	0
Pethidine	4	1·0	2·3	3·5	4·9	5·7	6·5	0	2·3	3·2
Promethazine	2	1·1	2·6	4·0	4·7	5·2	6·0	1·2	3·5	3·7

TABLE II.—*The Fall in Rectal Temperature that Occurred After Covering with Ice for 90 Minutes amd the Amount of Shivering that Occurred During the Last Hour of the Cooling Expressed as a Percentage of the Observations Made Under Similar Conditions with Basal Narcosis Alone*

	Percentage of Similar Readings with Basal Narcosis Alone	
	Fall in Rectal Temperature at 90 min.	Amount of Shivering, 35–90 min.
Recognized methods of facilitating the production of hypothermia:		
(*a*) Deep narcosis	+75	−95
(*b*) Curarization	+83	−85
(*c*) "Lytic cocktail"	+100	−95
Individual constituents of the "lytic cocktail":		
(*a*) Chlorpromazine	+104	−100
(*b*) Pethidine	+25	−42
(*c*) Promethazine	+15	−2

in facilitating the production of hypothermia is chlorpromazine. Pethidine, while moderately effective in eliminating shivering, has comparatively little effect in aiding the fall in temperature. The effects of promethazine appear to be negligible. A graphic representation of the rate of temperature fall obtained with chlorpromazine, pethidine, and promethazine (Fig. 4) demonstrates a steady fall in temperature with chlorpromazine. In the case of pethidine and promethazine the onset of shivering causes a marked

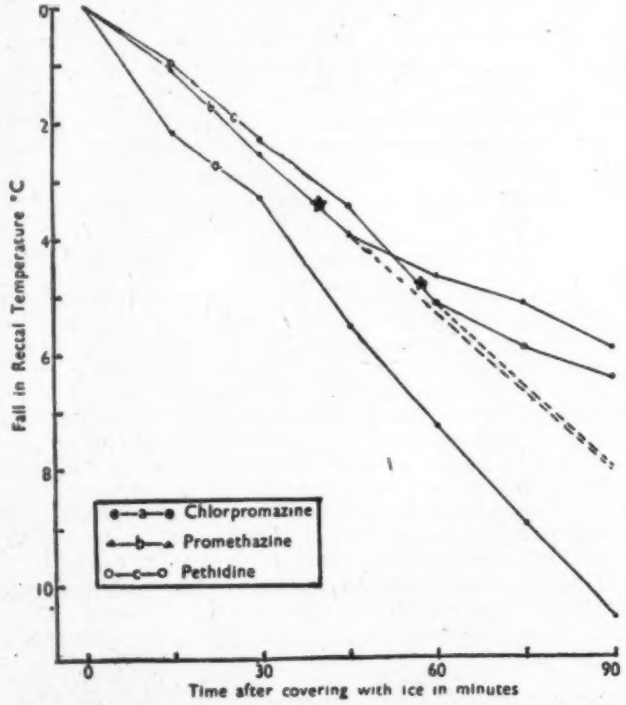

FIG. 4.—Rate of fall of rectal temperature when animal was immersed in ice with (*a*) chlorpromazine, (*b*) promethazine, (*c*) pethidine. * Average time after beginning of cooling to onset of shivering. ---- Hypothetic continuation of the steady fall in temperature that occurred with pethidine and promethazine before the onset of shivering.

reduction in the rate of temperature fall. A hypothetical continuation of the steady fall occurring before the onset of shivering shows that neither of these drugs would have been as effective in facilitating the fall in temperature as chlorpromazine. A possible explanation of this may be the occurrence of clinically undetectable shivering. That this can occur has been shown by previous electromyographic studies (Göpfert and Stufler, 1952).

It is not the purpose of this paper to consider the mode of action of these drugs in facilitating hypothermia, but one point, however, seems worthy of mention. A dog in which hypothermia has been induced with the aid of pethidine will show a very marked increase in the degree of shivering following the intramuscular administration of n-allyl-normorphine (3 mg./kg.). It is interesting to conjecture whether this is due to a reversal of the analgesic effect of pethidine in regard to thermal sensation (Evans, 1952) or whether it is due to a reversal of its central effects.

The fall in oxygen intake which we have observed during hypothermia closely resembles that reported by Bigelow *et al.* (1950). He induced hypothermia by cooling dogs sufficiently anaesthetized to eliminate shivering, and made no use of the "lytic cocktail." It is difficult to make a comparison with the findings of Churchill-Davidson *et al.* (1953), as these workers do not give sufficient details of their method of measuring oxygen consumption.

This could suggest that, provided shivering be eliminated, a fall in oxygen intake occurs with hypothermia irrespective of how this is produced.

Summary and Conclusions

A study has been made of the production of hypothermia facilitated by (1) deep anaesthesia, (2) curarization, (3) the "lytic cocktail." All three appear to be equally effective.

The active constituent of the "lytic cocktail" appears to be chlorpromazine. Pethidine decreases shivering somewhat while producing but little fall in temperature. Promethazine seems to have little effect.

Observations have been made on the effect of hypothermia on oxygen intake, pulse rate, and respiratory rate. All three are depressed at lowered temperatures, irrespective of how these are obtained.

We are indebted to Pharmaceutical Specialities (May & Baker) Ltd. for liberal supplies of chlorpromazine and promethazine used in this investigation.

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The Scientific Film Association has issued a catalogue of films on psychology intended primarily to help in the selection of films for research workers and senior students, teachers of psychology, and lay audiences. The films, of which there are 107, were made between the years 1930 and 1953, and all are believed to be available in the United Kingdom. About 70 of them have been appraised by methods evolved by the S.F.A. during the last 10 years, and the appraisals are included in the catalogue to help in selecting films. The catalogue is divided into seven sections: (1) Developmental Psychology, (2) Educational Psychology, (3) Testing Techniques, (4) Industrial and Applied Psychology, (5) Animal and Experimental Psychology, (6) Abnormal Psychology and Psychiatry, and (7) Juvenile Delinquency. Information is included on the running times of films, whether they are talkies or silent, and whether in black-and-white or in colour. Some are available free and others must be hired, and some are available only for special types of audience—that is, from which laymen are excluded. The catalogue lists many films made in Canada and the U.S.A. as well as Great Britain, and includes some made in Denmark, the U.S.S.R., Belgium, and Germany. While the Scientific Film Association itself does not distribute the films, the catalogue gives a list of owners and distributors from whom they may be borrowed. It is obtainable from the association at 164, Shaftesbury Avenue, London, W.C.2, price 7s. 6d. (8s. 1d. post free). It may be of particular interest to teachers of psychiatry.

HIBERNATION ANAESTHESIA IN MAJOR SURGERY

A REPORT OF 36 CASES

BY

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In major surgery, particularly in the case of malignant disease, where the patients are often cachectic and very ill, it is often not possible to contemplate surgical intervention. If an operation is started, after an hour or two of traumatic surgery the patient's condition deteriorates, and, however carefully the cardiovascular system is supported by intravenous transfusions, a state of shock develops. The completion of the operation may become an urgent matter, and the extent of the operation may have to be modified. Under effective "hibernation" anaesthesia the patient does not react in any way to the surgical stimulus, however severe or long-continued. Furthermore, intravenous transfusion is confined to replacing only the volume of blood lost. This is surprisingly small when measured, amounting to 300–400 ml. in extensive pelvic clearances. The body temperature drops to between 95 and 96° F. (35 and 35.6° C.), but this is only an indication that the autonomic blockade has succeeded, and it returns to a degree or two above the pre-operation level in six hours. The state of the patient approaches in many ways that found in the mammiferous hibernating animal, but it is not a truly comparable condition.

The defence mechanisms of the body for the preservation of the *milieu intérieur* of Claude Bernard against stress, aggression, or change in the external environment are largely the function of the autonomic nervous system. The hypothalamus, with its connexions with both the cerebrum and the autonomic system, has thus a large part in the control of the internal environment.

Conventional methods of anaesthesia attempt to modify these autonomic defences. This is done by depressing the cerebral functions, and in this way modifying the thalamic and hypothalamic control of the autonomic system; or, working from the periphery, by obtunding the stimuli that call the defence mechanisms into action. In the vasomotor system the defence mechanism, working through the mediation of the autonomic nervous system, causes the shutting of the pre-capillary sphincters and the opening of the arteriovenous shunts (Chambers *et al.*, 1943). This increases the circulating blood volume and also increases the venous oxygen tension, in order to combat the aggression. In the central nervous system, experimental work would indicate that the shunt mechanisms are not present; consequently, following aggression the oxygen supply to the vital centres is not diminished and may even be increased. In the peripheral circulation, if the stress is at all long-continued, these same defence mechanisms result in capillary dilatation, and the increased pressure at the venous end of the capillary loops is followed by fluid loss into the tissues, with diminution of the circulating blood volume. This leads to anoxia, building up of acid metabolites, and, finally, atony of the peripheral vessels—the fatal peripheral failure which no amount of intravenous or intra-arterial infusion will reverse. In this way the patient dies as a direct result of his attempt to preserve his *milieu intérieur*.

Physical Cooling

For many years attempts have been made to modify the reaction of the body to surgical aggression by means of physical cooling. It has been found by Prec *et al.* (1949), Bigelow *et al.* (1950), and Bigler and McQuiston (1951), and others that when the body temperature has been finally reduced by physical means the oxygen consumption of the tissues is markedly lowered. It is then possible to undertake surgical operations requiring the exclusion of the heart, or lungs, from the circulation for several minutes, without anoxic damage to the tissues.

However, the application of ice-packs, refrigerated blankets, and other external cooling in itself constitutes a stimulus which calls the defence mechanism into action. This is shown by increased oxygen consumption and heart rate, and by shivering in order to maintain body temperature. Only when the defence mechanism is overcome do the body temperature and the oxygen consumption drop (Prec *et al.*, 1949; Jaulmes, 1953). It is at this stage, on the way to final dissolution of the subject, that these operations can be performed.

The artificial hibernation technique evolved by the French workers, Jaulmes, Laborit, Huguenard, and others owes little to physical cooling of the subject from without, but depends on the specific neuroplegic effect of drugs, mainly those of the phenthiazine group on the autonomic nervous system. The phenthiazine derivatives include the antihistamine drugs promethazine hydrochloride ("phenergan") and promethazine-8-chlortheophyllinate ("avomine"), which has a central action, particularly upon the vomiting centre, and chlorpromazine ("largactil"), which has no antihistaminic action. This drug seems to act centrally on the autonomic system as a neuroplegic, and it has a pronounced anti-adrenaline effect and a direct depressant action on the temperature-regulating mechanism.

Laborit *et al.* (1952) have described a detailed plan for producing a state of artificial hibernation which has guided us in our efforts to ameliorate the condition of patients subjected to major surgical procedures. He relies on the use of a "lytic mixture" consisting of 50 mg. of promethazine, 50 mg. of chlorpromazine, and 100 mg. of pethidine, which is administered intravenously in divided doses in the hour before operation. The hibernant state is maintained by giving, intravenously, one of three "cocktails" containing, among other drugs, aneurine, pethidine, promethazine, chlorpromazine, diethazine hydrochloride, sparteine sulphate, ascorbic acid, ethyl alcohol, and procaine. In addition acetosterandryl, neostigmine, and heparin are given intramuscularly.

Present Investigation

We have attempted, so far as is practicable, to avoid the polypharmacy of our French colleagues. The technique which we now adopt and which has given excellent results in our hands in a variety of major surgical procedures is as follows. The patient is given 50 mg. of promethazine-8-chlortheophyllinate by mouth two hours pre-operatively. One hour later this is followed by a subcutaneous injection of 100 mg. of pethidine with 1/150 gr. (0.43 mg.) of hyoscine hydrobromide. The patient is brought to the anaesthetic room and the mixture of promethazine, pethidine, and chlorpromazine, in the proportions advocated by Laborit, is given in divided doses in the half-hour preceding operation. During the injection the pulse rate rises at first but later settles to a level a little above the resting rate, and remains unaltered despite the duration or severity of the surgical procedure. The respirations become shallow and may increase in rate, while the systolic blood pressure tends to fall and is maintained in the region of 100 mm. Hg. At the conclusion of the injection the patient is somnolent and apathetic but can still be roused. A small dose of 5% thio-

pentone, 2–3 ml., is given to produce unconsciousness, and tracheal intubations may then be performed with ease.

The patient is transferred to the theatre, where small doses of relaxants are given when required. Oxygen is administered if the respiratory excursion is inadequate, particularly in those cases requiring the steep Trendelenburg position. In prolonged operations, if the pulse rate begins to rise we have been able to re-establish control by a small supplementary dose of the original mixture. Great care is taken to replace any blood lost, as the patient is not able to compensate for gross diminution or increase of circulation blood volume. Our experience so far has been of patients aged from 28 to 76 years, and has included the following operations: gastrectomies, Wertheim's hysterectomies, hysterectomies, total colectomies, anterior pelvic exenterations, adherent malignant ovarian cysts, laminectomies, bilateral mastectomy and a second operation of prostatectomy on the same patient, together with less extensive operations in patients who would normally be considered poor risks.

Case Reports

Case 6.—A married woman aged 76, weighing 8 st. 4 lb. (52.6 kg.), had had two operations for carcinoma of the body of the uterus. She was admitted for symptoms of large-bowel obstruction with a large tumour arising from the pelvis with ascites. B.P. was 180/120. Six hours after admission she developed gross cardiac irregularity and electrocardiography indicated a coronary infarction. She was thought to be unfit for operative intervention. Two days later her condition became grave and fibrillation was occurring at a rate of 140, with a pulse deficit of 10–20 beats at the wrist. She was treated by the technique described above. Operation entailed the removal of a large adherent malignant ovarian mass involving the sigmoid colon, which was resected, and an anastomosis was performed, with a colostomy above. During the operation, which took three hours, she received 400 ml. of blood to replace the estimated loss. Her pulse rate remained irregular throughout at 90–100 a minute. Her rectal temperature was 96° F. (35.6° C.) at the conclusion of the operation. She was rousable within three hours of the end of the operation and regained consciousness after six hours. Her rectal temperature rose to 100.2° F. (37.9° C.) during this period and her pulse rate remained irregular at the same rate. She has made an uneventful recovery.

Case 23.—A man aged 46, weighing 8 st. 6 lb. (53.5 kg.), had generalized Paget's disease with involvement of the spine. He had had spastic paraplegia and loss of sphincter control for eight months. A myelogram showed a spinal block at the level of the fourth dorsal vertebra. We obtained an autonomic blockade by the method described, and an extensive decompression of the spinal cord was undertaken by performing a bilateral laminectomy from the fourth to the eleventh dorsal vertebra. Blood loss was very rapid and was replaced by a transfusion of 4 pints (2.3 litres). His pulse remained steady at 90–100 a minute and his systolic pressure was sustained at just over 100 mm. Hg. Recovery was uneventful and his neurological condition was improving.

Conclusions

It is impossible to assess statistically the advantages of any anaesthetic technique. From the small series of 36 cases involving really major surgery we have been impressed by the excellent condition of the patients, however extensive or long-continued the operation. We have had no deaths due either to the use of the method or to the operations performed. At no time during any of the procedures or during the post-operative period has the condition of the patient caused any anxiety. Furthermore, there has been no post-operative vomiting, nausea, or headache. The patients require less nursing care than normal, heavy post-operative sedation is not required, and there have been none of the post-operative complications which might have been expected to follow such major surgery. The patients are contented with this technique, for, although they can be roused, most of them have complete amnesia from the time they leave the ward until six to eight hours after the operation. The freedom from post-operative pain and restlessness during this period seems to aid their recovery, for when the autonomic blockade has worn off they are cheerful, rested, and relatively free from pain.

The great advantage of this modification of Laborit's technique has been that we are now able confidently to undertake the anaesthetic care of patients who previously would have caused great anxiety, or would have been considered unfit to withstand major surgical intervention.

Summary

A brief account is given of a simplified method of producing autonomic blockade, as a method of preventing surgical shock during and immediately after major operations. The patient's condition has been better, both during and after the operation, than when conventional anaesthetic techniques have been used.

We would like to thank our colleagues and the nursing staff of the hospitals at which this work has been done for their sustained interest, and also Messrs. May & Baker Ltd. for supplying the drugs used.

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THE BACTERIAL CONTENT OF HUMAN SMALL INTESTINE IN DISEASE OF THE STOMACH

BY

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It has already been shown (Cregan and Hayward, 1953) that when the human intestinal tract is healthy the small intestine is not colonized by a resident flora. Such organisms as are found there are so few in number that they must be regarded as transient contaminants passing through with the ingesta. The present work was undertaken to determine the effect of disease of the stomach on the flora of the small intestine. The results showed that neither a low gastric acidity nor the presence of a profuse flora in the stomach necessarily lead to the development of a resident flora in the small intestine. The antibacterial mechanism operating in the small intestine is therefore independent of the gastric germicidal barrier.

Experimental

The patients chosen for the experiment were undergoing operation for gastric or duodenal ulcers or gastric carcinoma. In addition, there was one patient with a subtotal gastrectomy of two years' standing and a small oesophageal hiatal hernia. He was operated on for recurring haematemesis and melaena. All had been given light nourishment and had then fasted for at least four hours before the operation.

The methods of collection and bacteriological examination of specimens and evaluation of results were exactly as previously described (Cregan and Hayward, 1953), and are stated only briefly here. The contents of the intestine were removed directly through the bowel wall with syringes. Thus the possibility of contamination was reduced to a minimum, the levels of the intestine sampled could be anatomically defined, and parts of the intestine remote from the diseased stomach but exposed during the operation could be sampled. A standard bacteriological procedure was followed with all specimens so that results could be assessed quantitatively as well as qualitatively, the degree of growth being graded from ± to +++. It was shown (Cregan and Hayward, 1953) that + or ± growth indicated a transient flora and that ++ or +++ growth indicated a resident flora at the site sampled.

Results

Twenty-two cases were included in the investigation, and in each case the sites sampled were the upper jejunum, the mid-gut, and the lower ileum within 8 to 12 in. (20 to 30 cm.) of the ileo-caecal sphincter. In addition the stomach was sampled in all but four cases. The quantitative results are shown in Table I and the qualitative results in Table II.

Effect of Gastric Acidity and of Profuse Contamination of the Stomach

Of the 14 cases in which gastric acidity was determined, seven showed normal acidity or hyperacidity. The stomach, the upper jejunum, and the mid-gut were either sterile or contained only a transient flora in all of these seven cases. The lower ileum was colonized by a resident flora in three of them. These findings do not differ significantly from those in normal subjects. The remaining seven cases in which gastric acidity was determined showed hypoacidity or achlorhydria. In four of these (Cases 8, 9, 10, and 11) the flora of the small intestine did not differ from normal, and in the other three both the stomach and the upper jejunum contained a resident flora, but by the time the intestinal contents had reached the mid-gut their bacterial content had been reduced to a transient flora. It is apparent that the subnormal gastric acidity of this group of cases did not affect the normal ability of the small intestine to prevent multiplication of bacteria in its lumen and to destroy large numbers of bacteria entering it from a heavily contaminated stomach.

Of the eight cases in which gastric acidity was not tested, six were of advanced gastric carcinoma and almost certainly had a low gastric acidity. The results from this group confirm the finding that when large numbers of bacteria enter a normal small intestine from a diseased stomach they are destroyed by the time the mid-gut is reached, if not earlier. In only two of the seven cases in which the stomach contained a resident flora (Nos. 17 and 21) did the profuse contamination persist even as far as the upper jejunum.

Cases 9 and 10, with only a transient flora in the stomach, indicate that lowered gastric acidity, even achlorhydria, is not necessarily accompanied by an increase of bacteria in the stomach.

Qualitative Results

The qualitative results are shown in Table II. As in the study of cases in which the intestinal tract was normal, the organisms found in the upper intestine in the present investigation were predominantly Gram-positive species of the general type more commonly associated with the mouth than with the lower intestinal tract. However, Gram-negative species of faecal type were found more often in this study, and in Table I a resident flora is designated oral or faecal in type. It must be noted that this designation is not intended to suggest the origin of the organisms.

In any one patient there was a correlation between the species found at each level of the tract. There was no apparent association between particular species and the disease or the general condition of the patient. In particular, *Candida albicans*, which has been said to be commonly associated with carcinoma of the stomach, and the toxin-

TABLE I.—*Quantitative Results*

Case No.	Gastric Acidity	Date	Disease	Operation	Stomach	Upper Jejunum	Mid-gut	Lower Ileum
1	Hyperacidity	13/7/51	Carcinoma of lower oesophagus invading stomach	Partial oesophagectomy. Total gastrectomy	−	−	−	−
2	,,	6/7/51	Duodenal ulcer	Subtotal gastrectomy. Billroth I	±	±	±	+ (F)
3	,,	2/10/52	,, ,,	Subtotal gastrectomy	−	−	−	−
4	Normal	17/4/52	Duodenal ulcer. Pyloric stenosis	,, ,,	N.T.	−	±	−
5	,,	13/5/52	Duodenal ulcer. Small perforation and perigastric abscess	,, ,,	±	−	±	+ (F)
6	,,	12/9/51	Laparotomy	Gastrotomy. Biopsy of stomach	N.T.	±	±	+ (F)
7	,,	11/7/52	Gastric ulcer	Subtotal gastrectomy	±	−	−	±
8	Hypoacidity	13/4/51	Gastric ulcer	Subtotal gastrectomy	N.T.	±	−	+ (F)
9	,,	22/6/51	Large high gastric ulcer	Total gastrectomy	±	−	±	−
10	Achlorhydria	10/6/52	Huge gastric ulcer penetrating liver and pancreas	Subtotal gastrectomy	±	±	−	−
11	,,	4/5/51	Extensive carcinoma of cardia and upper end of stomach	Total gastrectomy	N.T.	±	±	±
12	,,	13/2/52	Advanced carcinoma of cardia of stomach; peritoneal deposits	Abdomino-thoracic exploration. Souttar's intubation	+ (O)	+ (O)	±	±
13	,,	30/4/52	Carcinoma of gastric fundus invading pancreas and diaphragm	Laparotomy	+ (F)	+ (F)	±	+ (F)
14	,,	9/7/52	Haematemesis and melaena following subtotal gastrectomy for ulcer two years prevously. Oesophageal hiatal hernia	Total gastrectomy. Repair of diaphragm	+ (F)	+ (F)	±	+ (F)
15	Gastric acidity not tested	24/10/51	Advanced carcinoma of stomach with peritoneal spread	Laparotomy	+ (O)	±	−	+ (F)
16	,, ,,	10/10/51	Advanced carcinoma of upper stomach. Peritoneal invasion. Liver metastases	Oesophago-jejunal anastomosis (short-circuit)	+ (O)	±	±	+ (F)
17	,, ,,	24/7/51	Advanced gastric carcinoma. Peritoneal spread and metastases	Laparotomy	+ (O+F)	+ (O+F)	±	+ (O+F)
18	,, ,,	18/5/51	Gastric carcinoma. Pyloric obstruction	Subtotal gastrectomy	+ (O)	±	±	N.T.
19	,, ,,	29/8/51	Carcinoma of cardia and upper stomach	Left thoraco-abdominal. Total gastrectomy. Splenectomy	−	−	−	+ (O)
20	,, ,,	2/7/52	Extensive gastric carcinoma invading oesophagus	Total gastrectomy. Partial oesophagectomy. Splenectomy	+ (O)	±	±	±
21	,, ,,	20/3/51	Double gastric ulcer. Gastritis	Subtotal gastrectomy	+ (O)	+ (O)	±	+ (F)
22	,, ,,	2/10/52	Gastric ulcer	,, ,,	+ (O)	−	−	+ (O)

−=Sterile. ±=Transient flora (± or + growth). +=Resident flora (++ or +++ growth). N.T.=Not tested. O=Flora of oral type. F=Flora of faecal type.

formers, *Cl. welchii*, *Str. pyogenes*, and *Staph aureus*, were closely watched, but their presence had no apparent significance.

TABLE II.—*Qualitative Results*

Site of Sampling	No. of Subjects	Gram-positive Species	Gram-negative Species
Stomach	18	*Str. mitis* (16) " *acidominimus* (1) " MG (2) " *uberis* (2) " *salivarius* (1) " sp., variety 2 (1) " *pyogenes* (1) β-haemolytic streptococcus, not Groups A, B, B, or G (2) *Str. liquefaciens* (1) *Staph. aureus* (2) " *lactis* (3) " *saprophyticus* (1) *Lactobacillus* sp. (1) *Bacillus* sp. (1) *Cl. welchii* (4) *Candida albicans* (4) " *krusei* (3) *Monilia parapsilosis* (2)	*Bact. coli*, type I (5) " " Intermediate, type I (2) *Bact. aerogenes*, type I (1) " " II (1) *Paracolon* sp. (1) *Pseudomonas* sp. (1) *H. influenzae* (1)
Upper jejunum	22	*Str. mitis* (19) " MG (4) " *uberis* (1) " *salivarius* (2) " s.b.c. (1) " sp., variety 2 (1) β-haemolytic streptococcus, not Groups A, B, C, or G (1) *Str. faecalis* (2) *Staph. aureus* (2) " *lactis* (5) " *saprophyticus* (2) *Lactobacillus* sp. (4) *Bacillus* sp. (1) *Cl. welchii* (3) *Candida albicans* (3) " *krusei* (3) *Monilia parapsilosis* (2)	*Bact. coli*, type I (5) " " Intermediate, type I (1) *Bact. aerogenes*, type I (2) " " II (2) *Paracolon* sp. (1) *Pseudomonas* sp. (1) *Veillonella gazogenes* (1)
Mid-gut	22	*Str. mitis* (13) " MG (5) " *acidominimus* (1) " *salivarius* (2) " sp., variety 2 (1) " *faecalis* (1) " *durans* (1) *Staph. aureus* (1) " *lactis* (3) " *saprophyticus* (1) *Lactobacillus* sp. (1) *Bacillus* sp. (1) *Cl. welchii* (3) " *multifermentans* (1) " *butyricum* (1) *Candida albicans* (1) *Monilia parapsilosis* (1)	*Bact. coli* type I (4) " " Intermediate, type I (1) *Bact. aerogenes*, type I (1) *Pseudomonas* sp. (1)
Lower ileum	21	*Str. mitis* (8) " MG (3) " *salivarius* (5) " sp., variety 2 (1) " s.b.c. (4) " *pyogenes* (1) β-haemolytic streptococcus, not Groups A, B, C, or G (2) *Str. faecalis* (2) " *liquefaciens* (1) *Staph. aureus* (2) " *lactis* (2) " *saprophyticus* (2) " *afermentans* (1) *Lactobacillus* sp. (3) *Cl. welchii* (6) *Corynebacterium* sp. (2) *Candida albicans* (1) " *krusei* (1) *Monilia parapsilosis* (1)	*Bact. coli*, type I (8) " " Intermediate, type I (5) *Bact. coli*, Intermediate, type II (1) *Bact. aerogenes*, type I (5) " " II (1) *Paracolon* sp. (7) *Pseudomonas* sp. (2) *H. para-influenzae* (1) *Achromobacter* sp. (1)

Discussion

In all these 22 patients undergoing gastric operations the mid-gut (lower jejunum or upper ileum) yielded at most a transient flora, although in 10 of the cases the gastric germicidal barrier was defective and the stomach was heavily contaminated. Even in the case of subtotal gastrectomy of two years' standing in which there had been prolonged reduction of stomach secretions the mid-gut yielded only a transient flora (actually ± growth). The other cases show that advanced disease of the stomach, with associated physiological and anatomical changes, does not encourage the development of a resident bacterial flora in the small intestine. Therefore an antibacterial mechanism, distinct from that of the stomach, must operate in the small intestine. Failure to recognize that there are two independent mechanisms and that the stomach mechanism may be defective and the small intestine mechanisms be intact has led to the widely held misconception that if the gastric secretions are reduced or absent organisms from the large bowel will invade the small intestine. For example, Wells and Welbourn (1951) state that achlorhydria following gastrectomy causes "bacteria which normally inhabit the colon to grow freely all the way up the small intestine and in the gastric stump." This view has arisen from studies of samples, generally only from the duodenum and the stomach, removed by passing a tube via the mouth (Knott, 1927; Ricen, Sears, and Downing, 1928; Torrey, Kahn, and Salinger, 1930; Dick, 1941, quoted by Bethell *et al.*, 1942; French and Thompson, quoted by Frazer, 1949).

The results reported here show that a consideration of a single specimen from the upper small intestine could be misleading. The upper jejunum was heavily contaminated in 5 out of 10 cases in which the stomach contained a resident flora (Table I), but the scarcity of organisms further on in the mid-gut in all cases showed that this was not due to an invasion from the large intestine but to an abnormally heavy intake of organisms from the diseased stomach. In all cases reported here the antibacterial mechanism of the small intestine was functioning, whether gastric acidity was increased, decreased, or normal.

Further, this misconception has led to the suggestion that vitamin-B deficiencies in the post-gastrectomy syndrome (Welbourn, Hughes, and Wells, 1951; Wells and Welbourn, 1951), in the sprue syndrome, and possibly also in pernicious anaemia, pellagra, and nutritional megalocytic anaemia (Frazer, 1949) arise because bacteria invading the small intestine deprive the host of vitamins. This suggestion cannot rest on the fact that the stomach secretions are deficient. Until it has been shown that the small intestine's antibacterial mechanism is defective in these cases the theory has no sound foundation.

The work of Sinek and Reimann (1931) supports the findings reported here. They found that low gastric acidity was not necessarily associated with an increase in the incidence of *Bact. coli* in the duodenum.

More recently Barber and Franklin (1946), who examined swabs taken from the stomach and duodenum during stomach operations, found that, although the stomach was infected in 25 out of the 50 cases they examined, the duodenum was infected in only seven. They do not draw special attention to this fact, and the misconception has persisted in spite of their work.

No indication of the factors that determine whether a resident flora is established in the lower ileum can be seen from this work. Whereas 12 out of 21 cases yielded a profuse ileal flora in these cases of disease of the stomach, only 2 out of 14 did so when the intestinal tract was normal (Cregan and Hayward, 1953).

Summary

In cases of disease of the stomach presenting for operation the small intestine was found to contain only a sparse transient population, irrespective both of gastric acidity and of the degree of contamination of the stomach.

It is deduced that the small intestine has an antibacterial mechanism which is independent of the gastric germicidal barrier.

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TREATMENT OF ACUTE PANCREATITIS WITH HEXAMETHONIUM BROMIDE

BY

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In 1889 Fitz described three types of acute pancreatitis—haemorrhagic, gangrenous, and suppurative—based on the gross pathology of the gland. McWhorter (1932) collected 64 cases and classified them as follows: (1) acute or subacute pancreatitis in which there was no haemorrhage but in which the gland was enlarged, oedematous, and very hard; (2) the haemorrhagic, in which haemorrhages were present but there was no evidence of gangrene or suppuration; (3) cases with gross necrosis or gangrene but no suppuration; and (4) cases with suppuration or definite abscess formation.

A classification on an aetiological basis suggested by McWhorter (1932) and Jones (1943) adds little to our knowledge.

A. *Infectious Origin.*—(1) By extension along the lymphatics; (2) by extension from the blood stream; (3) by extension along the pancreatic ducts, from the duodenum or from the bile ducts; (4) by direct extension from infected foci; (5) following activation of bacteria in the normal gland; (6) by bacterial permeability from adjacent diseased viscera.

B. *Non-infectious Origin.*—(1) Mechanical, including stasis in the ducts. (2) Chemical, and originating in activated ferments resulting from (*a*) bile; (*b*) duodenal contents; (*c*) degenerated duct contents; (*d*) autolysis. (3) Degenerative changes in the pancreas: (*a*) secondary to benign or malignant tumours; (*b*) resulting from vascular degeneration or haemorrhage; (*c*) toxic changes following systemic disease. (4) Trauma.

C. *A Combination of Two or More of the Above Factors.*

The disease most commonly occurs in the fifth and sixth decades in obese males. Bisgard and Baker (1940) pointed out the frequent association of cholelithiasis. The disease may affect the whole gland or may be limited to the head, the body, or the tail. The extent of necrosis depends upon the violence of the biochemical explosion. If small areas alone are involved they may be absorbed or converted into fibrous tissue; but, if large, the necrotic areas soon slough or suppurate.

Ian Aird (1949) states that "a complicated network of theory has been woven around pancreatitis in order to relate it to gall-bladder disease but without any conclusive or all-embracing theory." We believe that pancreatitis is due to a vascular accident and that the findings of biliary pathology are coincidental.

One of us was impressed with the similarity in pathology of thrombosis and embolism in other organs, and treated with systemic heparin two cases of acute pancreatitis confirmed by exploratory laparotomy. The results were satisfactory, but led to a continuous ooze of blood from the suture line in each case. Although pain was relieved the loss of blood from the suture lines was sufficient to require intravenous blood transfusion. We concluded that the systemic heparin may have been responsible for the recovery of these two cases, which we classified, according to McWhorter's criteria, as gangrenous lesions of part of the head.

The following two cases were treated with hexamethonium drugs, and had a very smooth convalescence.

Case 1

An obese male aged 64 had been in good health until the morning of May 5, 1952, when he was seized with a sudden agonizing abdominal pain. It was located around the umbilicus and the left flank.

On examination he was found to be very shocked, and was frequently vomiting small amounts of bile-stained fluid. His face was livid and beaded with sweat, and the extremities were cold and damp. The abdomen was uniformly rigid, with maximum tenderness around the umbilicus. No other abnormal physical signs were discovered. A provisional diagnosis of pancreatitis was made. This was confirmed by exploratory laparotomy. The relevant findings were an injected peritoneum and a hard oedematous dusky-red pancreas with darker patches in the head. The proximal 3–4 in. (7.5–10 cm.) of the small gut was distended and scattered and traced with lymphatic vessels. The omentum revealed fat necrosis. The biliary tract was normal on palpation. The abdomen was closed without drainage.

The day following exploratory laparotomy the patient remained in great pain, and for this reason a bilateral posterior splanchnic block was performed with 1/2,000 amethocaine. The relief from pain was dramatic and the improvement in the clinical condition most marked. Pain began to return after complete control for approximately six hours. It seemed reasonable to believe that ganglion-blocking agents, such as hexamethonium, would similarly relieve pain, and that administration of this drug would have none of the difficulties or dangers of repeated splanchnic blocks. Oral hexamethonium bromide, 250 mg., was given via the indwelling Ryle's tube twice a day, and the activity of the drug was observed by blood-presssure readings, carried out by the nursing staff. Pain disappeared after six hours, and the next day it was possible to assess the patient as convalescent. Treatment with hexamethonium was continued for five days, the patient being discharged, cured, on the tenth day. He remained well up to the time of submitting this report.

Case 2

This patient was a man aged 52. His history was complicated by a previous perforation of a peptic ulcer six years previously. Three years before his present illness he was subjected to gastrectomy, this being followed by a complete remission of his indigestion.

On the day of admission (August 9, 1952) he was seized with violent upper abdominal pain, mainly localized to the right hypochondrium. He frequently vomited small amounts with each severe attack of pain, which appeared to be colicky in type. The abdomen was explored and a considerable quantity of free sero-sanguineous fluid was found. The great omentum was studded with islets of fat necrosis and several feet of the small intestine was injected, distended, and traced with lymphatic vessels. The pancreas was hard, oedematous, and of a deep-red colour over the whole visible surface of the gland. The biliary tract felt normal on palpation. The abdomen was closed without drainage.

Hexamethonium, 250 mg., was given as soon as the patient was conscious, and this was continued twice a day for the next seven days, four-hourly blood-pressure readings

again being carried out by the nursing staff. The following day he was pain-free, and convalescence was smooth and uneventful. He was discharged fit and well 12 days after operation.

Discussion

The treatment of acute pancreatitis has previously been based on its frequent association with cholelithiasis. It is our opinion that the findings of biliary calculi are coincidental, and that the pathological changes in the gland can be explained wholly in terms of a vascular catastrophe. The more serious or fulminating lesion can be explained by thrombosis or embolism of a main pancreatic vessel. Certainly the appearance of the gland at operation is supportive evidence, but the picture is clouded by the biochemical action, which releases a sanguineous or sero-sanguineous fluid rich in pancreatic ferments. If small areas only are involved they may be absorbed, converted into fibrous tissue, or calcified. It is impossible to reverse a pathological process which has involved sloughing or abscess formation, and this parallel may be seen in the upper or lower limb when embolism or thrombosis occurs in a main vessel. Survival of an organ depends on the location of the thrombosis or embolism, the state of the collateral vessels, and the presence or absence of vasospasm.

It is reasonable to suppose the same vascular phenomena take place in the pancreas, but the exact nature of the process must remain a matter of conjecture.

Andrew Dale (1952) reported optimistic results from the treatment of acute pancreatitis with splanchnic blocks. Our own experience of a single case before this publication supports his findings, but the mode of action is not understood. Ganglion-blocking drugs seem to produce an excellent result. The disease is robbed of its terrorizing pain. It, of course, cannot affect the established gangrenous or suppurative process in a gland which must be subjected to drainage.

In our experience exploratory laparotomy is indicated even if there appears to be no doubt about the diagnosis, as an assessment of the degree of destruction of the gland is then possible, and in the case of gangrenous, sloughing, or suppurative lesions drainage of the gland is indicated. Associated cholelithiasis should be ignored unless the pathology can be directly related to "inflammatory changes" in the pancreas. The inflammatory changes bear a striking resemblance to thrombosis or emboli of the main vessels to other intra-abdominal organs and the upper and lower limbs. Gangrene, sloughing, and suppuration follow gross disturbances of the blood supply, and the severity of the symptoms may be related to the extent of the infarction.

We feel, however, that types 1 and 2 of Fitz's classification might well be treated with drugs of the methonium group. In the cases reported hexamethonium was chosen arbitrarily. Each member of the methonium group varies in effect from ganglion to ganglion, and it may well be that some other member of the group would have a more pronounced action on the splanchnic ganglion. Paton (1951) suggests that tetramethonium may have this action.

In our two cases the relief of pain and the improvement in the general clinical condition were contrary to previous experience. We feel that a vascular catastrophe is the causative factor in acute pancreatitis, and further investigation along these lines may lead to a better understanding of the disease and simplify the treatment.

ADDENDUM.—Since submitting this paper for publication two further cases have been treated with equally successful results. *Case 3*, a man aged 62, admitted with severe abdominal pain, general collapse, and urinary diastase of 75. Diagnosis was confirmed by exploratory laparotomy, and he was treated with hexamethonium bromide. He was discharged on the tenth post-operative day and has remained free of symptoms for five months. *Case 4* was that of a man of 72 with typical acute abdominal pain. The urinary diastase was 68. Exploratory laparotomy confirmed the diagnosis, and treatment with hexamethonium relieved him of his pain. He was discharged from hospital on the twelfth day and has remained free from symptoms for four months.

We are grateful to Mr. Edward Muir for his interest and co-operation.

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LOCAL EFFECTS OF CERTAIN MEDICAMENTS ON THE TEETH

BY

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It is a common experience for dental surgeons to be confronted by small children, aged from 2 years upwards, suffering from gross caries of their deciduous dentition. This condition may arise from a variety of causes, and it is often difficult to decide what is the principal factor in a particular case. If, however, a child known to have normal dental structures suddenly develops rapid decay affecting particularly the labial and buccal surfaces of his teeth, the possibility of chemical damage must be considered. It has been observed that such damage often occurs after the protracted use of some of the commonly used iron tonics.

Certain of these iron tonics are very acid. Representative samples, tested with a Cambridge *p*H meter, gave the following hydrogen-ion concentrations:

	Undiluted *p*H	Diluted to 50% with water *p*H
Syr. ferr. phosph. co.	1.5	1.9
Mist. ferr. sulph. pro infant., *N.F.*	1.67	2.28
Elix. ferr. glucon., R.F.H. ..	3.52	3.8
Mist. ferr. et ammon. cit., *N.F.* ..	6.66	7.7
"Colliron"	8.56	8.87

The deleterious effect of acids on the teeth is well known. McClelland (1926) showed that teeth left in a solution of *p*H 4.5 for twelve hours suffered some degree of decalcification, and Stafne and Lovestedt (1947) reported many cases of dental damage following the prolonged and regular sipping of pure lemon juice (*p*H about 2.5). Hardwick (1950) has demonstrated that the amount of enamel decalcification that occurs when a tooth is immersed in an acid solution does not depend entirely on the *p*H of the solution but also on the nature of the acid. For example, N/100 lactic acid, with a *p*H of 2.9, in some circumstances produced etching of the enamel, whereas N/100 hydrochloric acid (*p*H 2.0) did not.

A laboratory test to ascertain the effect on the teeth of certain stock iron tonics was carried out. Sound teeth were suspended for a week in the various liquids at blood temperature with part of the crown immersed beneath the surface. In this case the resultant degree of damage to the teeth was proportional to the acidity of the solution. Syr. ferr. phosph. co. caused the most damage, the exposed enamel flaking freely away from the cusps of the tooth. Mist. ferr. sulph. produced severe etching and decalcification of the enamel, which could be scraped off the surface with a finger-nail. Elix. ferr. glucon. produced very slight etching, with milky-white decalcified areas. No macroscopical effect was observed on the teeth immersed in mist. ferr. et ammon. cit. or colliron.

It is the custom to advise that some iron tonics, notably Parrish's food, should be taken through a straw or a glass tube, but this presents practical difficulties, and in small children the parent usually gives it undiluted from a teaspoon, the child sucking the liquid over his upper incisor teeth. If this practice is continued for long the teeth often present a typical clinical picture—decalcification of the labial surfaces of the upper incisor teeth, usually accompanied by dental caries. If, as is often the case, the tonic is sweetened with syrup, the risk of caries will be considerably increased. In severe cases the teeth eventually disintegrate, break off level with the gum, and leave roots that quickly become diseased.

Syrup *per se* has been observed to cause damage to the teeth. The original sugar dummy, where the parent wrapped a lump of sugar in a handkerchief and thrust it in the child's mouth, has been popularly superseded by the immersion of a rubber dummy in rose-hip or blackcurrant syrup before use, with frequent replenishments throughout the day and night. This, if continued for any length of time, results in a startling destruction of nearly all the teeth. The *p*H of a popular brand of blackcurrant syrup is 3.

It is not suggested that dental damage invariably follows the use of iron tonics. The amount of harm depends on the acidity of the tonic; on the frequency, length, and method of administration; and on individual susceptibility. But the regular introduction into the mouth of highly acid and syrupy fluids is obviously a potential risk to the dental structures.

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Medical Memorandum

Spontaneous Rupture of the Oesophagus Treated by Operation

Although, following Barrett's comprehensive review in 1946, the symptomatology of spontaneous rupture of the oesophagus is firmly established, failure of recognition remains the greatest impediment to successful treatment. If the diagnosis is made early, and immediate operative repair effected, the patient has an excellent chance of complete recovery. It is clear from recent reports, both British and American, that, in spite of the occasional survival of a patient after repeated thoracentesis, plus delayed drainage of the pleural cavity or of a localized abscess, the treatment of choice is immediate operation, and the transpleural approach seems preferable to the mediastinal one. To the growing list of successful cases the following is added.

CASE REPORT

On January 4, 1950, a manual labourer aged 53, without previous history of digestive upset, was admitted to hospital with the complaint of severe left-sided pain of six hours' duration. He had been celebrating the New Year holiday by an indulgence in alcohol much beyond his wont, and he felt rather seedy when he returned to work on the 4th. At the mid-day break he ate, without appetite, his lunch, and thinking that some beer might act as a stimulant he drank a pint, and felt, if anything, rather worse. He thereupon, in continued hope, had a second pint, and he had not long finished it when he felt sick, and brought up a large vomit of food and beer. He continued to feel uncomfortable and he retched violently, and as he did so was seized with a sudden excruciating pain in the left side about the lower part of the chest. He distinctly remembers that he had expected to vomit on this occasion, but did not in fact do so. The pain was so agonizing that he was almost struck to the ground. He was helped to his home, and six hours later, about 6.30 p.m., was admitted to hospital. The original pain over the left chest was still present, and it had spread across the epigastrium and through to his back between his shoulder-blades.

On admission he was pale, distressed, and sweating; his temperature was 96.8° F. (36° C.), pulse 112, respiration 22, and blood pressure 110/85. There were dullness and diminished air entry over the left lung base, and some tenderness but no rigidity in the epigastrium. He was originally thought to be suffering from pneumonia. At 10.30 p.m. his blood pressure had fallen to 98/70 and his pulse had risen to 150, while the left lung base was completely dull on percussion and breath sounds were absent. The left chest was needled and brown turbid fluid, smelling of beer, aspirated. No subcutaneous emphysema was observed. At this stage a diagnosis was made of spontaneous rupture of the oesophagus with perforation into the left pleural cavity, and arrangements were put in hand for operation, an intravenous plasma drip being set up. In spite of this and the administration of morphine, the patient continued in great pain and severe shock.

Operation was carried out at 1.30 a.m., the left thoracic cavity being opened through the bed of the eighth rib. About 2 pints (1.1 litres) of opaque brown fluid, smelling of beer, welled out of the pleural cavity and there was considerable contamination of the cavity with food particles. A ragged tear about 2 in. (5 cm.) long was found in the pleura over the lower end of the oesophagus, and a longitudinal tear about 1 in. (2.5 cm.) in length in the left postero-lateral wall of the oesophagus an inch or so above the diaphragm. The rent in the oesophageal wall was clean-cut and healthy-looking, the tissue around it greyish black and necrotic. It was notable that whenever the pleural cavity had been cleared of stomach contents the condition of the patient greatly improved. The rent in the oesophagus was easily repaired with interrupted catgut sutures, and the wound in the chest wall closed, the pleural cavity being drained through a stab wound.

The next day the patient's condition was satisfactory and it remained so. Fluids were allowed by mouth on the second post-operative day. Convalescence was somewhat retarded by a haematoma at the posterior end of the thoracotomy wound, and a slight purulent discharge from the stab wound, so that he did not leave hospital until February 1. On his discharge he felt reasonably fit but was troubled with a slight cough. He was referred back to hospital on February 17 because of increasing breathlessness and cough. *X*-ray examination then showed an abscess cavity in the lower lobe of the left lung. While the patient was awaiting admission to the thoracic unit he coughed up the contents of the abscess, and thereafter the pulmonary infection rapidly resolved. He returned to work in April and has been in full work since and in excellent health.

COMMENT

The history of the abortive vomit with sudden agonizing pain and collapse in a previously healthy man, the profound shock, only partially alleviated by plasma transfusion, the resistance of the pain to morphine, and the rapidly increasing dullness at a lung base suggested the diagnosis: the aspiration from the left pleural cavity of stomach contents confirmed it. The absence of clinical evidence of surgical emphysema may be accounted for by supposing that the gastric contents, having ruptured the oesophagus, very rapidly tore a large gap in the left pleural membrane, and that gastric contents and air found a readier egress into the pleural cavity than into the tissues of the mediastinum. This case supports the view that the best hope for patients with spontaneous rupture of the oesophagus is early operation, and that much time should not be lost in pre-operative attempts to overcome shock completely, for this end is unlikely to be achieved except by operation.

I wish to thank Dr. James Brown and Mr. David Proctor for making the diagnosis, and Dr. James Stewart for the excellent anaesthetic management of a very ill patient.

S. G. DAVIDSON, M.B., F.R.C.S.

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Reviews

RESEARCH IN WARTIME

History of the Second World War: Medical Research. Edited by F. H. K. Green, C.B.E., M.D., F.R.C.P., and Major-General Sir Gordon Covell, C.I.E., M.D., D.T.M.&H., D.P.H. (Pp. 387. 40s.) London: H.M. Stationery Office. 1953.

This volume of the official history of the second world war describes the achievements of medical research undertaken for purposes connected with the war and sponsored by the Medical Research Council, the fighting Services, and other Government departments. Although some purely clinical subjects are excluded, the field covered is wide, especially since some of the matters brought in have a tenuous connexion with the war effort, or belong largely to the periods before or after the war: examples are the Prophit survey, the vole bacillus vaccine, a survey of mycoses, partition chromatography, and the use of radioactive isotopes. There is an excellent account of work done by scientists in conjunction with Service personnel to improve the safety and efficiency of the combatant. The variety of this work and its influence even on the design of weapons and other equipment will surprise anyone not familiar with it. The prevention of infection in wounds and burns, the nature of shock, blast injury, the transfusion of blood and blood products, and "chemical defence research" (with emphasis on B.A.L.) also naturally find their place. Descriptions are given of the development of penicillin, of new methods for preventing or treating typhus and malaria, of studies of epidemic hepatitis and serum jaundice, hospital cross-infection, and air disinfection. A chapter is given to the nutritional studies on which our rationing system was so successfully based and to treatment of starvation as seen at such places as Belsen.

The book is full of interesting and unfamiliar information. How many people know, for instance, that whole serum was issued as tetanus antitoxin early in the war to save the time needed for purification, that portions of the International Standards for antisera were sent to Canada in 1940 for safety, that a passenger lost both hands from frost-bite after being ferried across the Atlantic in a bomber, that conscientious objectors were used for experiments on the transmission of scabies, that anaesthetized volunteers were used to determine whether life-saving jackets would safely support an unconscious man, or that the discovery of *Br. melitensis* infection in cattle once led to a suspicion of bacterial sabotage? Although many contributors were responsible, the editors have clearly played a large part in producing this volume, since its style is singularly uniform and lucid. It worthily places on record the achievements of perhaps the most fruitful period of research in our history, a period when every task was urgent and every first-class brain was ready to help in furthering it. Each chapter has an ample bibliography, and readers for years to come will find this a valuable work of reference.

L. P. GARROD.

INTRODUCTIONS TO GENERAL PRACTICE

An Approach to General Practice. By R. J. F. H. Pinsent, M.A., M.D.(Cantab.). With foreword by Sir Lionel Whitby, C.V.O., *M.C.* (Pp. 166. 12s.) Edinburgh and London: E. and S. Livingstone. 1953.

An Introduction to General Practice. By D. Craddock, M.B., Ch.B., D.Obst.R.C.O.G. With foreword by Sir Heneage Ogilvie, K.B.E., D.M., M.Ch., F.R.C.S. (Pp. 552. £2 2s.) London: H. K. Lewis. 1953.

These two books by obviously able and conscientious general practitioners are well worth reading.

Dr. Pinsent takes the young doctor through his first surgery and then introduces him to the office work of general practice, to his colleagues, and to his patients. The chapter on the mind of a doctor is full of wisdom and understanding. He puts in a plea for research and welcomes the College of General Practitioners. He demands the highest clinical standards and urges the young practitioner to get some professional work outside general practice so as to avoid letting his mind become hidebound. Dr. Pinsent has an observant eye and an inquiring mind. He knows precisely when to consult, when to send to hospital, and when to treat on his own. Perhaps for this reason he is slightly condescending towards consultants, though he correctly describes the etiquette of a domiciliary consultation. He is full of self-assurance and pride in his work. These are admirable qualities, but they may be the cause of stumbling. Even with open *x*-ray departments and pathological laboratories many practitioners admit that they consult not only to have a diagnosis confirmed but also to find out what is wrong or how to treat. It is no doubt useful to have guidance about the sort of condition which requires hospital treatment and the sort which should be treated at home, but it is unwise to make set rules. It is also unwise to give the impression that sending a patient to hospital relieves the general practitioner of all responsibility. Sending a patient to hospital should be like calling in a consultant. To consult, as Dr. Pinsent shows, is to share but not to shed responsibility.

Dr. Craddock has written almost a textbook. He discusses briefly and "tidily" the conditions commonly met with in practice, dealing more fully with mother and child and family planning. His wide knowledge will be the envy of his colleagues. His detailed account of the techniques and prescriptions used in practice will be invaluable to old and young. His style is didactic and his opinion sometimes open to criticism. Not everyone believes in the virtue of adrenaline cream. He, too, demands a high clinical standard and holds a firm belief in the value of the general practitioner not only as a physician but as a philosopher.

Such a textbook accentuates the difference between hospital practice and general practice. The difference exists, but, if there is a fundamental difference of method in, for example, history taking and clinical examination, there is a danger that general practice may come to have a mystique as well as a technique of its own. This will widen the gulf. Men such as registrars having been trained in hospital will not accept nor be accepted by the mysteries of general practice. Only the young men with little hospital experience will find an entrance. If that occurs there is something wrong either with medical education or with general practice.

These books will be helpful if they are used to crown but not to supplant the training and ideals learnt in a good medical school. General practice must advance in step with the advances of medicine, and these are made in hospitals. Only a close association with hospital work will enable a general practitioner to keep abreast. Only close association with general practitioners will enable the hospital to keep a sense of proportion and humanity.

C. W. WALKER.

MORE SOCIAL MEDICINE

Social Medicine. By S. Leff, M.D., D.P.H., Barrister-at-Law. (Pp. 297. 28s.) London: Routledge and Kegan Paul. 1953.

This volume is the first of a series integrated to form a survey of human biology, and to be written by a number of authors. It is intended to provide a guide for doctors and other health workers in the exploration of social medicine. The author defines social medicine, but, like so many others before him, fails to provide a definition which is both concise and clear. The preface envisages possible criticism of the book on the grounds of undue emphasis on environmental and social factors. Any criticism on that score would be quite unjustified: environmental conditions have been too much neglected in recent years by the medical profession, and any trend in the opposite direction is to be welcomed rather than deplored. The vast industry of the

author is obvious from the text, and from the long list of his sources, which are fully catalogued and carefully referenced. The index is comprehensive and accurate. The paper, printing, and binding are excellent.

Dr. Leff looks far beyond the frontiers of this country: his outlook on social medicine is international in character, and that is good. There is a tendency here and in America to be too engrossed in the work near at hand and to forget that it is the duty of the advanced and fortunate countries to provide the greatest possible help to the backward peoples of the world. This book gives many striking examples of appalling conditions in some countries abroad, and will help to make conscience less easy and effort in aid more intense.

The language at times lacks precision. Some of the statements are too sweeping: for example, "diabetes . . . is cured by an injection of insulin," and "asthma is caused by a spasm of the bronchioles, and is cured by drugs which relieve the spasm." It all depends on what is meant by "cured"—the chronic asthmatic might well argue wheezily about that. Then there is a statement that diphtheria immunization was not introduced into Great Britain until 1941; it was, in fact, commonly practised in this country so long ago as 1927, and in one English city alone 16,000 persons were immunized against diphtheria in 1935.

This book is well worth reading, but I am unable to commend it as unreservedly as I did the author's previous book on the health of the people.

C. METCALFE BROWN.

A HOMOSEXUAL'S VIEW

The Homosexual Outlook: A Subjective Approach. By Donald Webster Cory. With an introduction by Dr. Albert Ellis. (Pp. 326. 18s.) London: Peter Nevill. 1953.

The publication in an English edition of this book must be considered timely (perhaps almost too timely!) in view of the excited interest in the problem of homosexuality existing at present. The book is unique in the history of serious homosexual literature in the sense that it is a comprehensive sociological study written by a self-avowed homosexual, who is neither a physician nor a lawyer. The problem is therefore reviewed from the inside, as it were, as well as objectively. This approach is in a way advantageous, for no one can be held to be altogether detached and objective in dealing with an emotionally overcharged problem of this kind.

The appearance of *Sexual Behaviour in the Human Male* (the first volume of the Kinsey Report) came as a startling revelation to the public, lay and medical alike, of the vastness of the homosexual problem. This book provides information on the nature (rather than the extent) of the problem which will surprise the reader, even if he regarded himself as already knowledgeable. Mr. Cory maintains that, from the sociological point of view at any rate, homosexuality should be regarded and treated as an important minority problem in the same way as colour prejudice, anti-semitism, and anti-Catholicism in Protestant countries (and anti-Protestantism in Catholic countries), and similar problems that have to be dealt with. It is for that very reason that objective judgments are so seldom forthcoming, for the hostile emotions aroused in the majority groups at the worst vitiate sound evaluation, and at the best give rise to biased rationalizations.

As to the efficacy of analytical psychotherapy in any of its forms in the treatment of psychosexual inversion, the author maintains that well-established homosexuality can never be eliminated. All that it can serve to do is, in certain cases, to release whatever heterosexual potentialities there may be in the patient's make-up by freeing him from his irrational fears and guilt-feelings. While this may help in bringing about a more satisfactory social adjustment, it cannot be regarded as a "cure."

As to the moral-theological aspect of the question, many will find themselves in disagreement with the author; but this side of the problem should not be allowed to bedevil the reader's outlook, provided he consistently distinguishes between the concept of sin and that of crime, as all sound moral theologians should do.

Without comment I conclude this short review with a quotation from Dr. Albert Ellis's introduction: "All told, *The Homosexual Outlook* is by far the best non-fictional picture of the American homosexual and his problems that has yet been published. It is *must* reading for all inverts and for everyone who wishes clearly and fully to understand the question of homosexuality. It is a decidedly serious, honest, discerning, moving and creditable piece of work. Even those who most violently disagree with its views will find this volume to be stimulating and worthwhile reading."

E. B. STRAUSS.

VOMITING IN INFANCY

Les Vomissements du Nourrisson. By Emilio Roviralta. (Pp. 240; 80 figures. 1,800 francs.) Paris: Éditions Médicales Flammarion. 1953.

Vomiting in infancy has been described by a medical student as a headache to parents and doctors; and when this assessment is apt—as in some of the recurrent, cyclical, and chronic cases—the chief reason is uncertainty about the cause. Professor Emilio Roviralta, who has had a long experience of paediatric surgery in the Polyclinic of Barcelona, has done a notable service to clinical medicine, as well as to paediatric surgery, by preparing this study. He exposes and attacks some of the false teaching about vomiting in infancy, and pleads for accurate case-taking, careful clinical examination, and the more general use of radiography. This is the road leading to correct diagnosis, and therefore to appropriate treatment.

At many centres in Britain the advice tendered so skilfully and authoritatively by Professor Roviralta is already followed, and abnormal conditions such as partial hernia of the stomach, diaphragmatic hernia, chronic duodenal stenosis, broncho-oesophageal hernia, and oesophageal atresia, with their puzzling clinical symptoms, are well known and are considered in differential diagnosis. But even in these centres much could be learnt from reading and pondering over this book, which has the great merit of being based on the personal experience of a worker who thinks clearly and honestly. His conclusions are especially valuable because they have had to find their way through a finely critical sieve. There is emphasis on many points of practical importance: for instance, the radiologist should be specially experienced in paediatric radiology; the vomiting baby may choke himself by inhaling food; and to give barium to a baby whose oesophagus is stenosed is likely to be dangerous. These facts, and many others to which the author refers, should be more widely known, and the volume is likely to be of interest not only to the experienced paediatrician and paediatric surgeon but also to the younger clinician, who will be stimulated by the scientific integrity of the work and its presentation. Radiographs are published to illustrate the reports, and there is a long bibliography.

NORMAN B. CAPON.

Though thriving on decay and often the cause of it, the fungi have yet given man many priceless benefits; high among them are penicillin, ergot, and Château Margaux '29. A few species out of this great host of parasites and saprophytes cause diseases with which we are familiar; many more destroy crops and have on occasion brought starvation by causing potato famines; others, again, reduce dwellings to dust—dry rot having been at least the physical cause of the fall of the House of Usher. An excellent account of these ubiquitous and influential plants has now come from the pen of Dr. John Ramsbottom under the title *Mushrooms and Toadstools* (Collins, 30s.). He writes for the layman, though he does not stoop to popularize a serious study, giving a discursive and often amusing account of his subject, on which he is an international authority. Doctors with a bent for natural history will enjoy this book, and it may be particularly commended as a Christmas present. It is well produced and contains many beautiful illustrations in colour and monochrome.

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HYPOTHERMIA

In the past little attention has been paid to the fluctuation of body temperature in a patient undergoing a major surgical operation, but in recent months the increasing interest in induced hypothermia has raised the question whether the maintenance of a normal body temperature is desirable at all times. The fact that a fall in body temperature is accompanied by a corresponding reduction in the oxygen consumption of the tissues led to the suggestion that hypothermia might be helpful when, in cardiac and cerebral surgery, the interruption of blood flow to the vital organs is contemplated. Various methods have been proposed for reducing the body temperature in man. First, the temperature of the patient's environment can be lowered after routine induction of anaesthesia, controlled at such a depth as to prevent shivering. This reduction of temperature is achieved either by immersion in cold water,[1] by a draught of cold air,[2] or by a cooling blanket.[3] A second method is to create an artificial arterio-venous fistula and cool the blood during its passage through the fistula.[4] And, thirdly, French authors[5] have recently claimed that a combination of drugs—the "lytic cocktail," containing pethidine, promethazine ("phenergan") and chlorpromazine ("largactil"), which is thought to be the most active constituent—has a specific action on the thermo-regulating mechanism and autonomic system and thereby lowers the patient's body temperature.

Chlorpromazine has been developed from the alkylamine derivatives of the aromatic base phenthiazine. It is said to be almost completely devoid of antihistaminic activity, but it has several incompletely defined actions on the central nervous system, including central depression extending particularly to the vomiting centre and possibly to the sensory, motor, and autonomic activities of the thalamus and hypothalamus. In addition to exerting these central effects, chlorpromazine is reported also to be an antiadrenaline compound.

Elsewhere in this issue Dr. J. W. Dundee and his colleagues and Drs. A. Smith and J. G. Fairer report the first two series in this country of the use of the "lytic cocktail" as a new method of anaesthesia for poor-risk patients undergoing surgical operations. In both these series the majority of the operations performed were for either gynaecological or abdominal conditions. As the theoretical advantage of the use of hypothermia in such cases is based on the reduction of metabolism it is interesting to note that in Dr. Dundee's series the average fall in body temperature of 3.4° C. was accompanied by a fall of oxygen consumption of approximately 20%. In one patient the body temperature was reduced nearly 10° C., yet the oxygen consumption fell by only 10%. This case emphasizes the danger of shivering, even at such low temperatures, for if it is not properly controlled it must necessarily throw an extra load on the circulation and increase the risk of ventricular fibrillation. The fact that these drugs produce an autonomic blockade in man is confidently expressed by Dr. Dundee and his colleagues in the title of their paper, but they do not present any evidence to corroborate such a view. It is possible that their findings might be accounted for on the basis of depression of the central nervous system. The mortality of 20% (hypothermia being a contributory cause of two deaths) in this series of 25 cases is a salutary warning to other anaesthetists eager to use this technique, and note should also be taken of the incidence of post-operative complications, including vomiting, haemorrhage, prolonged hypotension, and a sudden fall in blood pressure. These findings by experienced observers make it easier to place some of the previous extravagant claims for this technique in their correct perspective. It is perhaps a pity that the Liverpool team did not study the use of chlorpromazine alone, for more knowledge of the actions of this much discussed drug is still needed.

In their studies on the use of hypothermia in animals Dr. Dundee and his colleagues made a number of interesting observations. First, whether they used deep pentobarbitone anaesthesia, light pentobarbitone anaesthesia and muscle relaxants, or the "lytic cocktail," they found that all three methods brought about approximately the same rate of fall in body temperature. Further, they concluded that the value of pethidine and promethazine ("phenergan") in reducing metabolism and preventing shivering was dubious. These findings might suggest that, provided sufficient depression of the shivering reflex was obtained, the "lytic cocktail" possessed no great advantage over more familiar methods of anaesthesia.

[1] Churchill-Davidson, H. C., McMillan, I. K. R., Melrose, D. G., and Lynn, R. B., *Lancet*, 1953, **2**, 1011.
[2] Beard, J., *ibid.*, 1953, **2**, 1099. (Letter.)
[3] Bigelow, W. G., Lindsay, W. K., Harrison, R. C., Gordon, R. A., and Greenwood, W. F., *Amer. J. Physiol.*, 1950, **160**, 125.
[4] Delorme, E. J., *Lancet*, 1952, **2**, 914.
[5] Laborit, H., Huguenard, P., and Alluaume, R., *Presse méd.*, 1952, **60**, 206.
[6] Swan, H., Zeavin, I., Blount, S. G., Jnr., and Virtue, R. W., *J. Amer. med. Ass.*, 1953, **153**, 1081.

Another recent paper on the use of hypothermia comes from Swan and his colleagues[6] in Denver. Their series comprised fifteen patients, mostly children, who had undergone cardiac operations while they were in a state of hypothermia, with body temperatures ranging from 21.5° C. to 26° C. Hypothermia was induced during anaesthesia (thiopentone—cyclopropane—ether) by immersing the patient in iced water. At operation the chest was opened and in thirteen cases the circulation was stopped for periods varying from 2 to 8½ minutes by clamping the venae cavae, the aorta, and the pulmonary artery. The heart or pulmonary artery was then opened and the operation performed under direct vision. By this method four cases of atrioseptal defect and nine cases of pulmonary valvular stenosis were repaired, with only one fatality. The authors claim to have made great progress in the prevention of two serious complications of operations on the open heart under hypothermia—namely, ventricular fibrillation, which is combated by the use of an injection of a solution of 0.5 mEq potassium in 2 ml., and coronary air embolism, which is prevented by complete immersion of the heart in saline at the time of the closure of the cardiotomy.

Such results from the use of hypothermia in cardiac surgery are the most encouraging that have yet been published. But knowledge of this subject is still not sufficiently advanced to justify the use of deep hypothermia in general surgery. Great caution must be used in the selection of cases, and one hazardous procedure, induced hypotension, should not automatically justify a further hazardous procedure, hypothermia. The method of lowering the body temperature may not be of great importance: further comparative studies between the usual anaesthetic techniques and the "lytic cocktail" in conjunction with physical methods of inducing hypothermia will be needed before the matter can finally be settled.

B.C.G. IN SCHOOLS

To many it must seem strange that official sanction has now been given[1] for the B.C.G. vaccination of older schoolchildren before the completion of an official trial designed to determine how useful such a scheme would be. But to appreciate the reasons for this development it is necessary to probe a little more deeply. In 1949 the Ministry of Health and the Department of Health for Scotland authorized chest physicians and others to use B.C.G. in tuberculin-negative persons in contact with tuberculosis, especially home contacts, hospital nurses, and medical students.[2] This limitation was placed because out of the vast schemes of vaccination abroad the only cogent scientific evidence that seemed applicable to the British scene was of its value in those peculiarly exposed to the disease, in whom it reduced the incidence at least of primary and early post-primary tuberculosis.[3,4] This first scheme has been working well, though in some areas, even now, the numbers vaccinated fall short of those that qualify. However, important questions on the true value of *mass* vaccination remained unanswered. Although there was no indication for vaccinating all tuberculin-negative persons, did any section of the population, not individually known to be in contact with cases of the disease, merit consideration? What degree of protection would be expected under ordinary conditions of life in an industrial community with a comparatively low and falling mortality, moderate morbidity, and fairly high living standards? How much emphasis relative to other antituberculosis measures should the authorities place on mass vaccination in the general campaign? Of all sections, children about to leave school and enter the industrial world seemed to call for attention. No adequate statistically controlled trial of B.C.G. (including random and not voluntary selection of persons to be vaccinated or left unvaccinated, and specific planning in advance rather than analysis in retrospect) had been made anywhere on such a group, and the desirability of remedying this deficiency had been repeatedly urged.[5] Only two countries—Britain and the U.S.A.—had the resources for a trial and were in the advantageous (or shameful, according to the point of view) position of not already having established widespread B.C.G. vaccination; if not seized, the opportunity would be lost.

Accordingly the Medical Research Council set up a Tuberculosis Vaccines Clinical Trials Committee under the chairmanship of Dr. P. D'Arcy Hart and with Ministry of Health representation. The committee planned a large-scale controlled trial both of B.C.G. and of vole bacillus vaccine (Wells) in secondary modern school leavers in the Home Counties and in and around Birmingham and Manchester, and the work was put in the hands of the Council's Tuberculosis Research Unit. Apart from discreet

[1] Ministry of Health Circular 22/53. See *British Medical Journal*, Nov. 14 1953, p. 1111.
[2] Ministry of Health Circular 72/49 and Memo. 322/B.C.G. See *British Medical Journal*, 1949, **2**, 29.
[3] Hyge, T. V., *Acta tuberc. scand.*, 1947, **21**, 1.
[4] Heimbeck, J., *Tubercle (Lond.)*, 1948, **29**, 84.
[5] *British Medical Journal*, 1949, **2**, 1278; Aronson, J. D., and Palmer, C. E., *Publ. Hlth. R p. (Wash.)*, 1946, **61**, 802; *Wld Hlth Org. techn. Rep. Ser.*, 1950, No. 7; and *Dis. Chest*, 1951, **19**, 110.
[6] Pollock, T. M., *Bull. Nat. Ass. Prev. Tuberc.*, 1953, **16**, 2.
[7] Palmer, C. E., and Shaw, L. W., *Amer. Rev. Tuberc.*, 1953, **68**, 462.
[8] Dahlström, G., and Difs, H., *Acta tuberc. scand.*, 1951, **25**, Suppl. 27.
[9] Aronson, J. D., and Aronson, C. F., *J. Amer. med. Ass.*, 1952, **149**, 334.
[10] *British Medical Journal*, 1952, **1**, 147.
[11] Stein, S. C., and Aronson, J. D., *Amer. Rev. Tuberc.*, 1953, **68**, 695.
[12] Dahlström, G., *Acta tuberc. scand.*, 1953, Suppl. 32.
[13] Ministry of Health Memo. 324/B.C.G.

and welcome information[6] that this research scheme started towards the end of 1950, that over 50,000 young people enrolled between then and the end of 1952, and that its machinery is running smoothly, we are unlikely to hear anything definite from this committee for several years. This is as it should be, since premature assessment of results of any statistical investigation of a protective in tuberculosis might be misleading. A controlled study of B.C.G. vaccination in schoolchildren and others on rather different lines had been initiated by the U.S. Public Health Service in 1947.[7]

Pressure to introduce B.C.G. vaccination in this country as a routine measure for all school leavers has not been lacking in the meantime. Some tuberculosis specialists and paediatricians argued that, even though the M.R.C. investigation was expected to give a quantitative assessment of the true value of the vaccine in present-day circumstances in Britain, the evidence from abroad justified this further action being taken forthwith. The reasoning of these advocates followed two lines: first, since contacts were already offered the vaccine here on the basis of acceptable evidence of efficacy, school leavers who were about to be exposed, in the mass, to an increased risk of contact with the disease might, by extrapolation, be expected to derive at least some benefit; secondly, a few of the recent mass vaccination studies abroad, comprising follow-up of unvaccinated along with vaccinated groups, are regarded as highly suggestive or more,[8 9] shortcomings[10] and differences in milieu notwithstanding. Admittedly a scheme in which every tuberculin-negative child in the appropriate age group was offered the vaccine could give no information on the latter's efficacy in the succeeding years unless the attack rate of tuberculosis proved to be nil—which could not be expected.[11 12]

Impressed by these lines of argument as representing a reasonable viewpoint—though not the only one—the Ministry of Health has now[1] offered all local health authorities in England and Wales additional supplies of B.C.G. should they wish to extend its use to children approaching their 14th birthday, while continuing the scheme of vaccination of contacts. At the same time a memorandum[13] giving a balanced review of the status of B.C.G. has been provided to assist the local authorities, but, wisely, no attempt is made to influence their individual decisions whether to take action or not. Those authorities who adhere closely to the favourable views already mentioned will undoubtedly go ahead, strengthened in their decision by the knowledge that the vaccine is harmless and that local and glandular complications are not troublesome in adolescents. If they do so, the Ministry urges that there should be no interference with the current M.R.C. investigation proceeding in certain areas (this should not happen, since the intake of children has been completed and the volunteers have left school). Other authorities will be more cautious, believing that there is no need for urgency in an improving tuberculosis situation; that it is better to wait two or three years for the results of the M.R.C. investigation concerned with this very problem; and that the exposure to which these young people will be subjected in their various occupations will, on the average, be so much more dilute than those of individual contacts covered by the first national scheme that the consequent protective benefit may be quite small. These authorities will in turn be strengthened in their decision by the preliminary report of the U.S. Public Health Service's controlled trial,[7] which states that a large proportion of the tuberculosis appearing in the first few years of their scheme was in the group initially tuberculin-positive and therefore not candidates for B.C.G.; so far the amount of tuberculosis occurring in the initial tuberculin-negative persons, whether vaccinated or not, is still too small to show if B.C.G. has been effective. This report concludes that at present the American studies "do not indicate that tuberculosis in this country would be more effectively controlled by adding mass vaccination programs." The decision facing each local health authority is thus far from easy, since the issue is unclear. It is known that some have already decided to take part in the new scheme, and others to postpone extension. Either course is probably in accord with the discharge of their responsibilities to the community.

INFECTION AND POLIOMYELITIS

At the World Health Organization conference on poliomyelitis held at Rome in September there was much discussion about the spread of infection and its prevention. The general public is naturally much concerned about this, and it is doubtful whether the medical profession, concentrating on treatment, has in Britain given enough attention to what is known of the infectivity of the disease and to preventing its spread. The belief is commonly held that, in an epidemic of poliomyelitis, virus is widely and indiscriminately spread throughout the population, and that a clinical case is a rare incident in an outbreak of mass infection. This view has been contradicted again and again by careful studies of infected communities, and there is no virological or epidemiological evidence to support it. On the contrary, these studies invariably show that the virus is spread by close contact and that the path of its spread, when it can be traced, is quite narrow. Adamson,[1]

describing a winter epidemic among Eskimos in Hudson's Bay territory, showed how the spread of infection from one settlement to another followed the movement of man across hundreds of miles of frozen snow. The nature of the country and the habits of the people sharpened the lines of this epidemic, but the same pattern can be traced in all types of communities. Silverthorne[2] described the investigation of outbreaks in Dufferin County, Ontario, a rural area of over 500 square miles with 14,000 inhabitants, most of them living in large farms and villages. When poliomyelitis broke out, a team of experts moved in and studied the problem by carefully inquiring into the habits and movements of all contacts. Out of 28 cases, close contact with a previous case was proved in 17; moreover, of the 28 cases, only 12 were frank clinical cases; the other 16 suffered from the "minor illness" and would probably not normally have been recognized as cases of poliomyelitis. Of 37 cases described by Casey,[3] 29 were paralytic, and all of them followed short visits to the vicinity of a previous case. Examples quoted so far refer to rural areas, but Casey and others[4] have described similar investigations in the centre of Chicago. When a case was reported, a block of dwellings round the patient was defined and all residents aged under 25 came under survey; their habits at work and play, especially for the three days before and after the onset of illness in the case, were scrutinized. For control, another block, at least half a mile away, was chosen for a similar survey. This method was called "intensive neighbourhood study." Among 66 persons regarded as contacts, 37 fell ill, 24 diagnosable as poliomyelitis; among 109 non-contacts in the block, 4 fell ill; and among 115 non-contacts in the control block, 5 fell ill. The contact was always a close one, usually in the family or among playmates. Pearson and others[5] studied household infection: in 127 households where there was no known contact with poliomyelitis, virus was isolated from 2 (1.6%); in 45 households with non-familial contact, virus was present in 8 (18%); and in 8 households where there was a paralytic case it was found in 6 (75%).

We must regard the family as an infected unit. The clinical case, although quite possibly a more efficient spreader of infection, is not a solitary victim of the virus: it can usually be shown by virus studies that all or most of the other members of the family are infected almost simultaneously.[6] How the family is first infected and how the virus spreads from one person to another are problems still not solved. The type of contact necessary is evidently the type of association that occurs in families, among playmates, at children's parties, and in neighbourly visits. Faecal and respiratory spread are both possible, and hands may be infected by both faecal and respiratory organisms.

Though the exact mechanism of transfer is still uncertain, it is clear that people inside the family infect people outside. Most of these people remain well though infectious, but some become ill with headache, sore throat, nausea, muscular pains, irritability, and malaise. These are the symptoms of the minor illness of poliomyelitis; they are not clear-cut, but, in a known contact, clear enough to suggest infection. How often these illnesses occur can be determined only by close inquiry, and we have mentioned above that Silverthorne reported 16 minor illnesses out of 28 cases. A problem worth looking into is how many cases admitted to hospitals during epidemics of poliomyelitis and finally diagnosed as "constipation and headache," "myalgia," and so on are in fact suffering from this poliomyelitis minor illness.

With all this knowledge, can anything be done to block the line of infection? Quarantine of contacts is the obvious attack, and Agerholm has vigorously pleaded for it.[7] But, if it is to be effective in this disease, all intimate contact with other people must cease. If children are excluded from school, they must also be excluded from playgrounds, sandpits, parks, alleys, and courtyards. If adults must not go to work, neither must they visit cafés, pubs, or cinemas. Can such restrictions really be enforced? In city life it is most unlikely; in the country similar restrictions are already accepted in outbreaks of foot-and-mouth disease. If compulsion is impracticable, persuasion and public opinion might be more effective. When a case occurs in a family, the parents should be told the facts and asked to co-operate. A simple illustrated pamphlet might help to secure this. During epidemics the public should be informed by press and poster of the dangers of *contact* infection. It is unlikely that intelligent parents would run risks. As Agerholm points out,[7] in 1950 people cancelled visits to the Isle of Wight of their own free will. If anything is to be achieved, public health policy must be based on facts: the parents of a paralysed child should no more be heard to say that "the health people have been round and disinfected everything." A good deal of what passes for contact supervision in the common infectious diseases has become a matter of dull routine, delegated to health visitors and sanitary inspectors. In poliomyelitis there is need for expert and inspired inquiry.

[1] Adamson, J. D., *Canad. med. Ass. J.*, 1949, **61**, 339.
[2] Silverthorne, N., ibid., 1949, **61**, 241.
[3] Casey, A. E., *J. Amer. med. Ass.*, 1942, **120**, 805.
[4] —— *et al.*, ibid., 1945, **129**, 1141.
[5] Pearson, H. E., *et al.*, *Amer. J. Hyg.*, 1945, **41**, 188.
[6] Zintek, A. R., ibid., 1947, **46**, 248.
[7] Agerholm, Margaret, *Lancet*, 1953, **2**, 287.

A NEW SYNDROME

The work of a pneumoconiosis medical panel might be thought at first to be restricted to routine duties in a narrow specialty and unlikely to afford opportunities for original observation, but it was in the course of his routine duties in assessing cases of pneumoconiosis for industrial injury benefit that Dr. A. Caplan[1] noticed a high incidence of rheumatoid arthritis associated with massive fibrosis in cases of pneumoconiosis. Of 51 cases with rheumatoid arthritis 90% showed massive fibrosis, whereas in 14,000 other cases of pneumoconiosis only 30% had massive fibrosis. On assembling the radiographs of the 51 cases Caplan further noticed that in a quarter of them the pulmonary shadows were of a peculiar and uncommon form. Instead of the usual gradual enlargement of irregular fluffy opacities to form large massive shadows, in these cases multiple, well-defined, round opacities 0.5–5 cm. in diameter appear relatively quickly, usually in the periphery of the lung fields on both sides. The background of simple pneumoconiosis is also less well marked than is usual in progressive massive fibrosis (P.M.F.). After they have appeared, these round shadows usually remain stationary, but sometimes enlarge slightly, may cavitate, and in long-standing cases show some signs of shrinkage. In three fatal cases tubercle bacilli were recovered from areas of massive fibrosis, and Caplan suggested that the joint changes might be a form of "tuberculous rheumatism."

Further epidemiological study was required to establish the validity of this special syndrome and to discover the real association between P.M.F. and rheumatoid arthritis, for the apparent association noted in compensation cases might have been due to a greater likelihood of men with both arthritis and P.M.F. to apply for disablement benefit than men with either alone. Fortunately an appropriate epidemiological instrument was immediately available for such a study, the results of which we publish this week at page 1231. In 1951 Dr. A. L. Cochrane, of the Medical Research Council Pneumoconiosis Research Unit, had *x*-rayed 95% of all the miners and ex-miners living in the Rhondda Fach.[2] In 896 of these men a radiographic diagnosis of P.M.F. or clinically significant tuberculosis had been made. From the films of these men Caplan selected 20 as showing the particular appearance which he thought would be associated with rheumatoid arthritis. A random sample (stratified for age) was taken from the films he had rejected, and similar control groups of cases with simple pneumoconiosis or normal films were also chosen. A physician unaware of the radiological diagnosis visited all these men at home to inquire about symptoms of arthritis. The men with a suggestive history were examined, and if necessary fully investigated to confirm the diagnosis. Of the cases selected by Caplan 11 (55%) were found to have rheumatoid arthritis, a proportion differing significantly from the 3% in the controls with P.M.F. or tuberculosis and none in the other controls. While this epidemiological work has not fully confirmed the association between rheumatoid arthritis and ordinary P.M.F.—for the prevalence in P.M.F. was only just significantly greater than in the normal controls—it demonstrated the reality of the special syndrome described by Caplan. It seems that, given a chest radiograph of a miner which shows the characteristic "rheumatoid" appearance, a diagnosis of rheumatoid arthritis may be made with rather more than a 50% chance of being right.

Among the 20 cases with the "rheumatoid" type of opacity there was a suggestion that arthritis was associated with slightly longer dust exposure, especially to stone dust. The Middlebrook–Dubos agglutination test was positive in 8 of 18 sera tested (44%), contrasting with only 3% of 133 cases of early P.M.F. Only one patient had a positive sputum, and in one elderly man who died there was no evidence of active tuberculosis, the round lesions being histologically similar to ordinary massive fibrosis. There is thus only a suggestion that the pulmonary lesions are tuberculous: the true pathological condition can be shown only by necropsy or biopsy study of recent lesions.

There seems to be no satisfactory explanation for the association between the lung and joint changes. The latter are quite typical of rheumatoid arthritis, unlike those found in hypertrophic pulmonary osteoarthropathy and fibroma of the lung. It seems unlikely that the lung shadows represent a modification by dust of rheumatoid changes occurring in the lung, for no such changes are found in the lungs of ordinary cases of rheumatoid arthritis.[3] However, rheumatologists do occasionally observe extensive pulmonary fibrosis in cases of rheumatoid arthritis, more chronic than that described by Ellman and Ball,[4] and similar lesions have been described in other collagen diseases.[5–8] Miall and his colleagues dismiss the possibility that the arthritis is a response to the pulmonary lesions acting as a "septic focus" because of the long interval that may elapse between the onset of each, and they favour a hypothesis that a deficiency of adrenocortical hormones may underlie both the arthritis and a modified response of the lung tissues to dust and infection. Now that this syndrome has been described it will no doubt come to be noted with increasing frequency. Unpublished cases have already been observed in men exposed to other dusts than coal. Miall and his colleagues have provided us with a striking example of the value of epidemiological study, on a defined and unbiased population, in revealing the existence of a syndrome first suspected from clinical observation. Their account, in an appendix, of the observer error encountered in subjective methods of assessment, both of radiographs and joints, should encourage other clinicians to follow their example and test their own abilities with the same critical courage.

1 Caplan, A., *Thorax*, 1953, **8**, 29.
2 Cochrane, A. L., *British Medical Journal*, 1952, **2**, 843.
3 Baggenstoss, A. H., and Rosenberg, E. F., *Arch. Path.*, 1943, **35**, 503.
4 Ellman, P., and Ball, R. E., *British Medical Journal*, 1948, **2**, 816.
5 Shuford, W. H., *et al.*, *Arch. intern. Med.*, 1953, **92**, 85.
6 Rakov, H. L., and Taylor, J. S., ibid., 1942, **70**, 88.
7 Foldes, J., *Amer. J. clin. Path.*, 1946, **16**, 160.
8 Baggenstoss, A. H., *Proc. Mayo Clin.*, 1952, **27**, 412.

SYNTHETIC OXYTOCIN

The first synthesis of a new group of biologically important substances calls for recognition by doctors as well as chemists. That of oxytocin, the principal uterine-contracting and milk-ejecting hormone, has lately been

reported by du Vigneaud and others[1] of the Department of Biochemistry, Cornell University Medical College. This is the first polypeptide hormone to be synthesized. But from a footnote to an accompanying publication[2] it appears that a similar success has probably been achieved also in the case of lysine vasopressin. The latter is a closely related hormone, and a synthetic polypeptide synthesized by similar methods to those used in the synthesis of oxytocin has been found to possess pressor and antidiuretic activity. Oxytocin can be thought of as a cyclic polypeptide and side-chain, with a cystine residue as its key component. Four other amino-acid residues are joined in a closed ring through cystine; they are, in order, tyrosine, isoleucine, and glutamic and aspartic acids (as amides). In a side-chain, attached to one arm of the cystine residue, are proline, leucine, and glycine (as amide). The deduction of this structure by chemical reasoning was perhaps the most important step in du Vigneaud's achievement. Its synthesis, with a first yield of 360 mg., is no mean accomplishment in organic chemistry.

The biological activity of the synthetic preparation has been confirmed, in respect of uterine contraction on an isolated rat uterus, and in respect of milk ejection on a human subject. The total activity, assayed by the chicken-depressor method, is 29,000 units, and the activity per unit weight has been compared with purified preparations of the natural hormone. Although chemical identity is not specifically claimed by du Vigneaud and his colleagues, the evidence for it is thus strong. The case of vasopressin is of further interest from the apparent existence of an inter-species difference in composition. From earlier work on purified natural preparations of hog (leucine) and beef (arginine) vasopressin it had been concluded these hormones differ from oxytocin only in the replacement of the leucine and isoleucine residues of the latter, in lysine vasopressin by phenylalanine and lysine, and in arginine vasopressin by phenylalanine and arginine. The difference between hog vasopressin and beef vasopressin is thus confined to a single residue—lysine in the one, and arginine in the other. Lysine vasopressin has been synthetically prepared, and shown to possess biological activity. A fuller report on this work will be awaited with interest, as also will the confirmation by synthesis of the inter-species difference. While there is usually a considerable gap between laboratory synthesis and practical production—and du Vigneaud's synthesis of oxytocin is laborious—the relatively good yield which he has obtained encourages the hope that supplies of synthetic hormone will eventually become available.

A FORGOTTEN CHAPTER

The new College of General Practitioners in its first annual report refers to a piece of forgotten history—the abortive attempt to found such a college just over 100 years ago. One statement is made, however, which, though literally accurate, may be misunderstood. In describing the movement to set up the college in the 'forties of the last century the writer says: "The British Medical Association showed itself in favour. A meeting held on November 26, 1844 (Dr. Webster, President, in the chair), resolved," etc. Actually Dr. Webster was never President of the British Medical Association as we now know it, but of an earlier, short-lived, and Ishmaelite body which had assumed that title in 1836, claiming to represent the medical practitioners of the United Kingdom. In 1844 the *Medical Times* reported the British Medical Association as having "met in the person of Dr. Webster on September 28. The secretary was absent, and the resolutions appear to have been moved by the president, seconded by the president, put to the vote by the president, and carried by the president. He was the whole meeting." It was not until 1856, ten years after the first British Medical Association had disappeared without trace, that the body which had hitherto been known as the Provincial Medical and Surgical Association became the British Medical Association.

Nevertheless, Dr. George Webster, a zealous medical reformer of his time, took a principal role in formulating the demand for a charter of incorporation for general practitioners. He was the principal figure at a meeting at Hanover Square on March 14, 1845, when "there were about 1,200 gentlemen present, including the most respectable general practitioners in all parts of London." From a letter by a "village surgeon" who attended the meeting we learn that there was also "a fair sprinkling of country practitioners, as many as, considering the sickly season of the year, and the constantly existing difficulty of locomotion inherent in our calling, could reasonably be expected." An attendance of 1,200 would be considered a bumper one in these days, even in times of medico-political crisis, notwithstanding a less sickly season and better means of locomotion. But, like many other events of this kind, it was only a firework display. Blunders were made in the election of the permanent committee, the draft charter of incorporation was sent to the Home Secretary without being submitted to another general meeting, the confidence of the profession was largely forfeited, and the enthusiasm petered out. The Royal Colleges, too, were not pleased at the use of the words "medicine" and "surgery" in the proposed title of the college. The Home Secretary at that time was the rather ineffective Sir James Graham, who had drafted no fewer than four Bills for the regulation of medical practice. In the last of these he introduced a proposal for a college of general practitioners, but it was a meaningless affair which would have been dependent upon the Royal Colleges.

The present movement has proved much more successful than that of 100 years ago, and the new College, which gained a membership of more than 2,000 before it had been in existence for six months, has been established with good will on all sides of the profession. It is now consolidating itself, building up regional faculties, and preparing to play a major part in the academic field both for general practice and for general practitioners.

[1] du Vigneaud, V., Ressler, Charlotte, Swan, J. M., Roberts, C. W., Katsoyannis, P. G., and Gordon, S., *J. Amer. chem. Soc.*, 1953, **75**, 4879.
[2] du Vigneaud, V., Lawler, H. Claire, and Popenoe, E. A., ibid., 1953, **75**, 4880.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

INFECTED URINE

BY

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One of the commonest reasons for suspecting a urinary infection is because the urine appears turbid, but this may, of course, be due to other factors than bacterial infection.

It is generally possible to decide fairly quickly whether or not turbidity is due to infection or to other causes. A turbidity which disappears on warming is due to urates only, but if the turbidity remains after the test-tube has been warmed then another sample should be taken and a few drops of acetic acid added, because a cloudiness which clears up with acetic acid only is due simply to phosphates. If the turbidity persists both after warming and after acidifying with acetic acid then it is probably due to pus, to blood, or to bacteria. Urine that is "bell clear" in appearance is very seldom infected.

Microscopical Evidence of Infection

The presence of infection is confirmed by the detection of pus or bacteria in the urine. An infected urine generally contains pus cells, and microscopical examination is the only way of identifying these. Chemical tests for pus are so insensitive and open to so many fallacies that they are hardly worth performing.

The simplest and quickest way of carrying out the microscope test is to take a drop of the urine and run it into the chamber of a Fuchs–Rosenthal slide, such as is used for the examination of cerebrospinal fluid. This differs from the ordinary blood-count slide in that it is ruled to enclose 16 mm.^{2} and has a depth of 0.2 mm., whereas the haemocytometer slide is only 0.1 mm. in depth.

If a drop of urine is pipetted into such a C.S.F.-counting chamber and allowed to settle it can be examined in a few moments, and microscopical examination will show at once whether or not the urine contains pus or blood. One great advantage of this method is that no centrifuging is necessary. Another is that one can decide at once whether the turbidity of the urine is due to pus, blood, bacteria, or crystals, and, if pus is present, roughly how much there is.

The more usual method of carrying out a microscopical examination is first to centrifuge the urine, then to place a drop of the deposit on an ordinary microscope slide, cover this with a cover-glass, and examine with the sixth objective. This is certainly the best method, but if no centrifuge is available the urine may be allowed to stand in a conical vessel for a few hours until a deposit has formed. After decantation of the supernatant urine a drop of the deposit is collected in a pipette and examined on a slide beneath a cover-glass.

Before passing on to bacteriological tests it is worth recalling that sometimes tests for pyuria may give an indication of the location of the infection in the urinary tract. The two-glass test is often sufficient for deciding whether pus comes from the urethra or the bladder. To perform this test the patient is asked to pass urine into two glasses. Pus present in the first glass is assumed to be derived from the urethra, and that in the second from the bladder or kidneys.

In suspected pyelitis or pyelonephritis and in some cases of renal tuberculosis it may be necessary to examine specimens of urine collected separately from the bladder and each kidney. A unilateral tuberculous lesion of the kidney gives rise to pyuria from the affected kidney, whilst the urine from the opposite kidney and the bladder is clear. Uncomplicated cystitis shows the presence of pus in the bladder urine, but the urine from each kidney is free from pus and sterile. When large quantities of pus are found in urine this is almost always due to cystitis. Pyelitis, pyelonephritis, prostatitis, and urethritis usually give rise only to a relatively slight degree of pyuria.

Collection of Specimens for Bacteriological Tests

Specimens of urine for bacteriological examination need to be collected with special care and to be examined as soon as possible. Catheterization is not always necessary. For male patients a mid-stream specimen collected after cleansing the urethral orifice is generally quite satisfactory for bacteriological tests. Catheterization is more often required with female patients; in fact, if urine from women is found to contain a few pus cells and bacteria a catheter specimen is generally necessary in order to decide whether or not infection is present. Naturally catheterization should be avoided if possible, and it is worth pointing out that with reasonable care a clean specimen can often be obtained from a woman patient. A preliminary examination of this may be enough to decide whether or not catheterization will ultimately be necessary. The collection of a "clean" specimen of urine from infants or young children is a task which may tax the ingenuity and resources of all concerned.

Microscopical Examination of Stained Films

The next step is the examination of stained films from the centrifuged deposit, and for the preparation of these a drop of the deposit is spread evenly over a microscope slide and allowed to dry. The film is then fixed with heat by passing it three times through a flame. All urinary deposits should be stained with Gram's method as a routine. The great advantage of this stain is that it distinguishes between staphylococci, which are Gram-positive and appear purple in the stained film, and gonococci, which are Gram-negative and stain red. It is useful also in distinguishing the common Gram-positive diphtheroids and Döderlein's bacilli from Gram-negative bacilli such as *Bact. coli*, etc.

Whether or not any other stains should be used depends on the nature of the case. If there is no reason to suspect tuberculosis or other unusual infection, it is not necessary as a rule to stain more films. On the other hand, if the Gram stain shows the presence of pus cells but no bacteria, or if tuberculosis is suspected, the films should be stained by one of the methods used for acid-fast bacteria. Tubercle bacilli are rarely found in large numbers in the urine, and it may take several minutes' search to find them in a stained film, but bacteria like staphylococci, *Bact. coli*, and other coliform organisms are present in such large numbers that they can be recognized by one glance at the stained film.

Bact. Coli Infections

Infection with *Bact. coli* is a common finding. It may give rise to infections of the kidney, bladder, prostate, or epididymis, each of which has its own distinctive symptomatology. When the urine is found to be infected with *Bact. coli* the next step is to discover which part of the urinary tract is affected. This may generally be decided from the clinical history and the results of physical examination, but in exceptional cases it can be determined only after the collection of urine from the bladder and each kidney separately.

Meanwhile the problem remains, why has the infection occurred? *Bact. coli* is a relatively harmless microbial species and rarely causes trouble in organs which are functioning normally, so it becomes the object of clinical examination not only to decide where the infection is located but also why this region is affected. Many *Bact. coli* infections of the urinary tract are unlikely to be permanently cured until some underlying structural or functional defect has first been removed. Special predisposing causes are peculiar to different periods of life, such as infancy, pregnancy, or the years when prostatic obstruction is apt to set in.

Urine infected with *Bact. coli* is hazy when passed and has an opalescent appearance. If the urine glass or bottle is held up to the light and rotated to circulate the urine, the haziness appears like a drifting mist, a very characteristic feature. This is caused by the innumerable bacteria suspended in the urine. The haziness of the urine varies in intensity in different samples, being most evident in the early-morning urine. Later in the day the urine may be almost clear. The hazy opalescent appearance is only found in samples of urine almost free from pus. If much pus or blood is also present it will cause a turbidity which conceals the characteristic appearance of a simple bacilluria. In some cases of *Bact. coli* infection the urine has a peculiar fishy odour, but this is not invariably characteristic. The faculty of smell is rarely used as an aid to diagnosis in any branch of medicine nowadays, and without being fastidious most of us would agree with the views of the seventeenth-century physician who wrote: "It is too base and sometimes dangerous for the physician to put his nose to the urine to discern the stench thereof."

Proteus and Pyocyaneus Infections

Urine infected with proteus has the same general appearance as in *Bact. coli* infections but may also contain a small quantity of viscid ropy mucus in which the pus cells are suspended. The reaction is usually alkaline, and triple phosphate crystals and amorphous phosphates are commonly found in the deposit.

Infections with proteus may occur either in the bladder or in the kidney and are generally of a more severe character than *Bact. coli* infections, and more difficult to cure. *Ps. pyocyanea* is found in the urine under similar circumstances to *B. proteus*. If pus is present in large quantity this may develop a bluish green colour on standing.

Staphylococcal and Streptococcal Infections

The presence of staphylococci in urine may be the result of chance contamination in collection, and it is common to find these and other bacteria in any stale specimen which has begun to undergo ammoniacal fermentation. In these circumstances, of course, the presence of staphylococci is of no pathological significance; but if they are recovered from urine which has been carefully collected and examined without delay the finding of these organisms is an important observation. Staphylococcal infections may occur in the kidney, bladder, prostate, urethra, and epididymis. They may be associated with calculous disease and provide evidence of both the existence and the nature of a stone. The examination of stained films from the centrifuged deposit of the urine is a test which should never be omitted in calculous disease. In stones associated with staphylococcal infections the films may show enormous numbers of Gram-positive cocci, though the bacteriological culture plates may yield only a few colonies. When the urine is infected with staphylococci or proteus, and is strongly alkaline in reaction, further tests should be carried out to see whether or not the infecting bacteria ferment urea. Most strains of staphylococci and proteus ferment urea and thus render the urine alkaline, leading to the precipitation of phosphates and calcium carbonate.

Streptococcal urinary infections are rare, but it is fairly common to find streptococci in the urine in mixed infections, especially in severe urinary sepsis associated with carcinoma of the bladder or vesico-colic fistula. Pure streptococcal infections of the urine may be found in cases of pyaemic abscess of the kidney and chronic urethritis and prostatitis.

Gonococcal Infections

Three laboratory tests may be used in the diagnosis of gonorrhoea—namely, microscopical examination of films, bacteriological examination of cultures for gonococci, and the gonococcal complement-fixation test. The film method is usually sufficient for the recognition of acute gonorrhoea, but in chronic infections it is best to make use of both films and cultures. This is especially important when the finding of Gram-negative diplococci in films is an unexpected observation, and also in tests for cure in chronic gonorrhoea. In all medico-legal cases all three methods of examination should be employed. These tests will be discussed in more detail in a later article in this series.

Urinary Tuberculosis

Three methods are available for the detection of tubercle bacilli in urine: stained films, cultures, and animal inoculation.

The film method is the easiest and requires least apparatus. It has the advantage that it takes only a few minutes to carry out, and so a report can be given without delay. The tubercle bacillus is the only pathogenic acid-fast bacillus likely to be present in the urine, and with proper precautions it is unlikely that a trained observer will report a false positive by mistaking one of the non-pathogenic acid-fact bacilli for the tubercle bacillus. The stained film is therefore the regular routine method of examination. If acid-fast bacilli having the typical morphological characters and staining reactions of tubercle bacilli are found in stained films in association with red blood cells and pus, then, as a general rule, no further tests are necessary, and the diagnosis of tuberculosis may be considered to be established. If acid-fast bacilli are found which are not quite typical in microscopical appearances, then it is best to reserve a final opinion until the results of the cultures are available, or until virulence tests have been undertaken. On the other hand, when acid-fast bacilli are found in a urinary deposit unaccompanied by blood cells or pus then it is always necessary to proceed to confirmatory tests before accepting these acid-fast bacteria as genuine tubercle bacilli.

Culture tests for tubercle bacilli are not difficult to carry out and are a routine procedure in hospital laboratories. They are useful for the further study of acid-fast bacilli of uncertain character found in films. They should also be undertaken in cases in which there is a possibility of a tuberculous infection although acid-fast bacilli have not been found in the stained films. In a small percentage of cases of urinary tuberculosis tubercle bacilli may be obtained from cultures when they could not be found by examination of films. This is because the pathologist can plant out on the culture media a much larger volume of urine than could be searched in a film; therefore, when tubercle bacilli are relatively scarce it is only to be expected that some cultures may be positive when the films have been negative.

Guinea-pig inoculation is the final court of appeal in tuberculosis, but it should not be resorted to unless other methods of diagnosis have failed. It is an expensive test, it takes at least three to six weeks to complete, and it involves an experiment on a living animal which, naturally, should only be undertaken with reluctance. Experience has shown that the guinea-pig inoculation test very rarely reveals the presence of tubercle bacilli which could not have been discovered by films or by cultures. In fact the culture method is probably a more delicate test than guinea-pig inoculation, especially when large quantities of the centrifuged deposit of urine are spread over several culture tubes. By this distribution of the centrifuged deposit it is possible to submit for examination a larger volume of urine than can be injected into one guinea-pig. However, there are certainly some occasions when animal-inoculation tests are indispensable—for example, in identifying suspicious acid-

fast bacilli recovered by culture, and in the examination of material which is limited in quantity and obtained with special difficulty, such as urine collected by catheterization of the ureters.

Sensitivity Tests

The range of antibiotics is steadily extending, consequently there is an increasing demand on the services of the laboratory for carrying out sensitivity tests in cases of urinary infection. It is well established that most staphylococci and streptococci recovered from urinary infections are sensitive to penicillin whereas *Bact. coli* and other coliform organisms are generally insensitive to penicillin, though often sensitive to chloramphenicol, aureomycin, or oxytetracycline. If the urine is infected with *B. proteus* or *Ps. pyocyanea* response to oxytetracycline or streptomycin may be expected in some cases. The laboratory control of chemotherapy will be discussed more fully later in this series.

Next article on Clinical Pathology.—"Tests of Renal Function," by Dr. R. I. S. Bayliss.

Refresher Course Book.—The first collection of articles in the Refresher Course for General Practitioners (fully revised) are available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

THE LIBRARY OF THE ROYAL SOCIETY OF MEDICINE

An extension to the library of the Royal Society of Medicine is being opened this week, on Friday, December 4, by the Marquess of Salisbury. The new library, which is to be called the Wellcome Research Library, has been provided through the generosity of the Wellcome Trustees. To celebrate this occasion we have pleasure in printing below an authoritative account by a special correspondent of the origin and growth of the library of the Royal Society of Medicine.

The Royal Society of Medicine was founded in 1907 following the amalgamation of a number of specialist medical societies and the Royal Medical and Chirurgical Society of London. Some of the special societies had built up collections of books, but the chief foundation of the library of the Royal Society of Medicine was the library of the Royal Medical and Chirurgical Society of London. It is impossible to neglect the history of the library of the R.M.C.S. in any account of the library of the R.S.M., and even to-day some of the library regulations of the parent society remain unchanged.

Foundation of the R.M.C.S. Library

According to the first minute of the meeting which led to the foundation, in 1805, of the Medical and Chirurgical Society of London it was "Resolved unanimously that a society comprehending the several branches of the medical profession be established in London, for the purpose of conversations on professional subjects, for the reception of communications and for the formation of a library." When the first secretary, John Yelloly, reported on "the dignified and important objects for which this society has been established" he placed high among them "the collection of an extensive and select professional library." A library committee was set up in 1806, when £100 was provided to buy books. Presentations were received, and by 1808 the library had about 500 volumes.

The First Honorary Librarian

In 1810 the Society moved from its first house at 2, Verulam Buildings, to 3, Lincoln's Inn Fields, which was shared with the Geological Society. The growth of the library was not forgotten at this time, for the Medical and Chirurgical Society obtained the right to erect bookcases in the meeting-room. Some members had already shown an interest in "arranging the library," and in 1812 Bateman was appointed honorary librarian; he thought highly enough of his office to mention it on the title-page of his *Delineations of Cutaneous Diseases* (London, 1817). James Atkinson in his *Medical Bibliography* has left this description of the first honorary librarian: "He was then [i.e., a year before Bateman's death] a spare, oblique, marasmoid figure, labouring much under disease, and a cornucopia of whims and self-possessions or conceits; but of a very irritable kind. He then gave me the idea that he never could have been the quiet discreet registrar of disease, which bears so much semblance in his works, and I confess that from the state of exuvium in which I saw him, I should have set him down for anything but a clever man—I mean, in science, as an *homo saturatim imbutus*. We must recollect, however, that when any man is unwell, it is not the time to take his portrait." Soon after his appointment, Bateman, in company with Yelloly, made a book-buying journey to Paris, and the library benefited greatly from this.

The first printed catalogue was issued in 1816. Two years later a supplement appeared and a library copy formed from these and kept up to date by the insertion of new entries remained in use for many years. This same period saw the establishment of practices which are still followed to-day. In 1817 the number of volumes which a member might borrow was raised to eight, though new books and journals less than a month old could not be borrowed. In 1818, with the appointment of Samuel Cooper to assist Bateman, the custom was established of entrusting the supervision of the library to two honorary librarians. A third point of present-day practice also dates from this time. It was ordered in 1816 that a written request from the member concerned must be presented by anyone claiming to be borrowing books on his behalf; this was after "a person unknown had taken out books in Dr. Goode's name."

In 1819 the Society moved to 30, Lincoln's Inn Fields, and in 1820 to number 57, where it remained for the next 14 years. There is no known record of the effect on the library of these repeated removals, but the occurrence of unusually high binding costs at this time suggests that the books suffered physical damage.

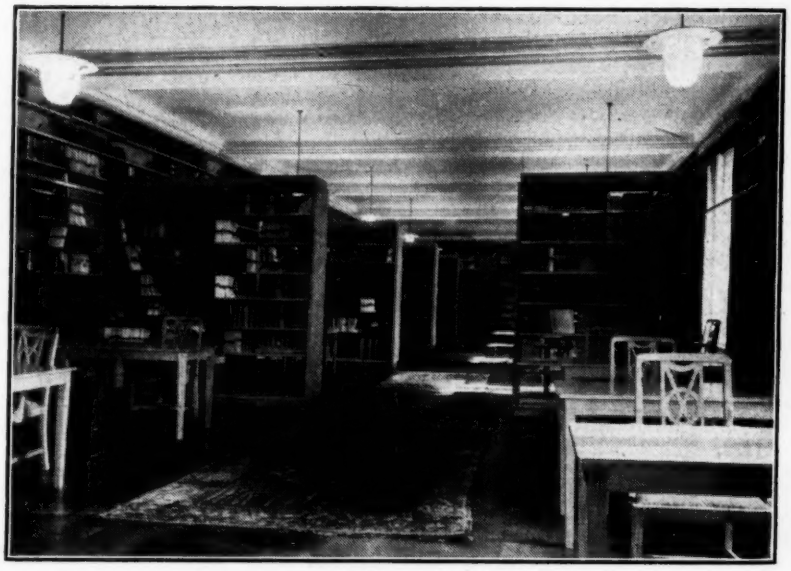
In 1822 the Council ordered that "all new English publications be sent in as soon as published, subject to their being returned to the booksellers, if presented by the authors to the Society." This practice was modified in 1826, when the Council ordered that books laid before it for approval should have been seen by one of the librarians and "sent forward with his sanction."

For some years it seemed to have been one of the duties of the resident clerk "to deliver out the books," but in 1832 an "assistant to the librarians" was first employed, apparently solely for library duties under the supervision of the librarians.

In 1835, when the Society moved to 53, Berners Street, a reviewer in the *Lancet* of April 23 made some harsh criticism of London medical libraries in his notice of Forbes's *Medical Bibliography*. He said of the R.M.C.S. library: "It is only lately that any French journals have been added: no German or Italian, or any other continental medical journal beside the French is now received. Only a minority of modern works, and those slowly, are procured. . . . The utmost ignorance of foreign medical literature evidently prevails among the managers." A new catalogue was started in 1837, and a copy was distributed to every Fellow in 1844. By 1847 storage space was giving concern, but the deficiencies in the collections were an even greater anxiety. A committee of 21 Fellows was created to inquire into these deficiencies and to prepare lists of books for purchase. As a result, 432 books (57 English, 153 French, 175 German, 5 Italian, and 42 Latin) were bought in 1848 at a cost of £253 10s. 9d.

A Great Bibliographer

In 1855 Benjamin Robert Wheatley, one of the great bibliographers, became sub-librarian. The library held about 17,000 volumes and was growing by annual increases of 500. One of Wheatley's first tasks was to provide an index of the library's possessions. This work, containing more than 35,000 references, was ready in manuscript in 1860. It had a double value: not only did it show what the library held; it also showed obvious gaps, and efforts were made to fill them by the immediate purchase of 150 works on botany and chemistry. The average daily number of readers in the library was 12. It seems that even at this time the library recognized the need for supplementing its own resources in order to satisfy Fellows, for in 1863 comes the first mention of a subscription being placed with Kimpton's circulating library. The growing awareness of the importance of the public health and epidemiological aspects of medicine was reflected in the policy of collecting sanitary and public health reports "for their value in illustrating results of sanitary measures on death rates and for the presentation of figures not available in the reports of the Registrar-General."



Interior of the Wellcome Research Library.

In the annual address in 1868 the President commented on the addition of 519 books, and continued, "with reference to what has been said of the library, I must add that every Fellow who requires a book which is not there, ought to enter it in the recommendation book, and, in all probability, the librarians will order it at once." The collections of periodicals, too, had been greatly enriched, and in the annual report for 1870 there is a note that at the general meeting "Dr. Webster made a few remarks as to the superiority of the Society's library to any foreign library he had ever seen in relation to the completeness of its journal collection."

Increase in Accommodation

In 1871–2 a new reading-room was built, giving space for 27,000 volumes, and for the first time the Society had library accommodation which was distinct from the meeting-rooms. With the new reading-room came a rearrangement of the books which it was hoped "would render the library as noted for convenience and ease of reference as it has long been for its value and extent." In the following session (1872–3) 3,171 books were lent, and 3,156 readers used the library. A contemporary comment on the increase in the Society's expenditure said that this "was partly due to a greater number of books of importance than usual having been brought before the Library Committee, but is greatly owing to the increasing growth in the number of important new foreign journals, which are much in request by the Fellows and constantly being added to the Library tables." With the new reading-room arranged, Wheatley turned to the preparation of his great three-volume catalogue and subject index of the library. Work began in 1874 and the catalogue was published in 1879. From the 17,000 volumes of 1860 the library had now grown to 31,000.

It is possible here to make only brief mention of the growth of the periodical collection as it appears from the catalogues of 1844, 1856, and 1879. A catalogue of 1844 has this manuscript note on a fly-leaf:

Library contains:	
Journals entered as such	49
Journals entered under other heads	190
Transactions entered as such	34
Transactions entered under various heads	133

It was the practice, followed in all three catalogues, to make a distinction between "Transactions," which indicated a periodical published under the auspices of some medical or scientific society, and "Journals," which covered periodicals issued without official support from any particular society. This 1844 catalogue is prefaced by a "list of the periodical publications which are to be found on the library tables, alphabetically arranged." The list is under two headings, British and Foreign. The British periodicals numbered 13, the foreign 10. By 1879 the total number of journals and transactions thus catalogued had risen to 177.

Although nine supplements to the 1879 catalogue, covering the years 1880 to 1901, were published, no new catalogue was printed thereafter. Such works are increasingly difficult to prepare and long delays in publication made the production of an up-to-date printed catalogue virtually impossible. In common with most other medical libraries, the Society's library has come to rely on the card catalogue of its own collections and to use such international bibliographical works as the Surgeon-General's *Catalogue* and the *Index Medicus* as guides to the literature. Nevertheless, in its day, Wheatley's catalogue of 1879 was a very valuable publication.

In 1881 he was given the title of resident librarian; in the next year an assistant was also employed in the library. Wheatley died in 1884. There were 93 applicants for the vacant post; the Council appointed James Bailey, of the Radcliffe, who remained for three years before moving to the Royal College of Surgeons, where he carried out a complete reorganization of the College library.

Sir John MacAlister

Bailey was followed by Mr. (later Sir) John MacAlister. His contribution to the progress of the R.M.C.S. and to the formation of the R.S.M. extended far beyond the library; yet to him, as a librarian alone, the Society owes a vast debt, whilst outside the Society he made a great name for himself in the little world of professional librarians and in the history of the Library Association. Although he was unable to accept the invitation, it is worth recalling that in 1905 MacAlister was invited to attend the International Library Congress in St. Louis as one of the representatives of European librarianship. At the time of his appointment about 3,900 books were borrowed annually and about 4,500 readers used the library. Storage space was becoming an acute problem. In the words of the president at that time, "every year there was increasing difficulty in placing the books of the constantly growing library. The room used for the Society's meetings, the council-room, and the committee-room all contained books." The Society moved to larger premises in 1889, at 20, Hanover Square, but three

years later further work had to be done there to give additional library space. In 1905 a new store to house 10,000 books was built behind the meeting-room. Even so, books were again invading the corridors.

It was not until MacAlister's day that the library "services" as well as the library collections received serious attention. Quite early in his term of office he made the library more accessible by an increase in the hours of opening. (By 1898 the library was open daily from 11 a.m. to 6.30 p.m.) In the *Lancet* of June 16, 1910, a letter appeared over his signature offering a service to provide abstracts and to undertake searches of the literature for Fellows living abroad. He wanted to make it as easy for "the man in the Andes" to benefit from the library as for the man in Wimpole Street. It was primarily to benefit the man who was unable to come and use the library himself that MacAlister planned library "services."

Amalgamation

In the first years of this century MacAlister was deeply concerned in the negotiations which, in 1907, resulted in the formation of the Royal Society of Medicine. The amalgamation brought several special collections of books to enrich the Society's library, of which the most extensive were the libraries of the Obstetrical Society of London (15,000) and of the Odontological Society (5,000). The Laryngological Society had placed its books in the care of the R.M.C.S. in 1902; the Ophthalmological Society of the United Kingdom, whilst maintaining its separate existence, deposited its library, under special conditions, in the new R.S.M. These additions not only filled gaps in the collection of the R.M.C.S. but also provided duplicate copies of many important early works. The benefit of this duplication has become increasingly apparent with the growth of the library's lending service.

Following the amalgamation, MacAlister carried through the building of the Society's house on its present site. This new building was opened in 1912.

In 1924 the room formerly known as the Marcus Beck Laboratory was handed over to the library, and, as the present Marcus Beck Library, houses a collection of historical works. The Society's historical collections had been greatly enriched in MacAlister's time by gifts from many Fellows, noteworthy among whom were Sir William Osler—he gave the library its only copy of the first edition of Harvey's *De Motu Cordis*—and Albert Chalmers, from whom came a valuable bequest of pamphlets and books which included amongst other rare items a fine copy of the *editio princeps* of Celsus's *De Medicina*. At this time, too, the modern books were arranged in a broad classification which brought collections of books together under a number of headings corresponding fairly closely with the interests of the various Sections of the Society.

Extension of Service

In 1925 the hours of opening were again extended. On Thursdays and Fridays the library remained open until 10 p.m. and was no longer closed during August, although late opening was suspended during that month. In the same year the service providing abstracts and bibliographies was officially extended to all Fellows. This year also marked the end of MacAlister's long term of service to the Society. He had been appointed secretary and consulting librarian in 1901, and throughout the period his influence on the development of the library, under its successive librarians, Archibald Clarke, C. R. Hewitt, and H. E. Powell, was of inestimable value. The library which he first directed in 1887 served 745 Fellows. At his retirement this number had grown to 4,000.

By the middle 'thirties the library had further grown under Mr. G. F. Home. He introduced a formal classification on the Brussels system; to its ever-growing collections of journals he added the most complete collection in the country of the great French and German encyclopaedic works. The scope of the journal collection was also increased. Most of the American State journals of medicine were included as well as a number of smaller hospital journals. Their value was derived mainly from the growing custom of reporting original work in them at an earlier date than would have been possible in the large national journals. The collection of sanitary reports was also increased as a result of efforts to collect the annual reports of all medical officers of health. A *List of Periodicals in the Library* complete to December, 1937, was published in 1938. The bibliographical services were maintained and arrangements made to file and preserve copies of all lists prepared and all translations made so that they remained as a source of information for all Fellows. Indeed, this service was almost too successful. Its usefulness produced increasing demands, with the result that the time-lag betwen the receipt of a request and its satisfaction became a pressing problem. In an effort to lessen inconvenience to Fellows a quick reference service was introduced, aiming at the speedy tracing of a limited number of articles to provide either an adequate review of a subject or a starting-point from which a Fellow can follow a subject in greater detail. This was indeed a period of rapid expansion, and at the time of his retirement Mr. Home left a greatly enlarged and enriched heritage to his successor, Mr. P. Wade.

By 1939 the library stock was approaching the 200,000 mark and space was again becoming scarce. Extra stacks had been erected in the basement and structural alterations made on the first floor to give more space.

The outbreak of war arrested the immediate demands on space, but inevitably brought its own problems. Some 40,000 of the rarer books and journals were moved out of London. They were stored so as to be available, and eventually provision was made for a small reading-room in this store. The main library also remained open. In addition to the photostat machine, microfilm apparatus was provided in order to copy material needed by Fellows in the Services; and microfilm readers were distributed, through the Army authorities, to establishments abroad. As in the first world war, the library was again opened to members of the Allied Forces.

After the war strenuous efforts were made to close the gaps in runs of important Continental journals. Once again an honorary librarian, Dr. T. C. Hunt, followed in the steps of the first honorary librarian, and made a Continental tour in search of material to complete the collections. Thanks to a generous grant from the Rockefeller Foundation, the Central Medical Library Bureau was set up and carried out extensive copying (from the Society's and other libraries' stocks) of out-of-print journals urgently needed by war-damaged libraries at home and abroad.

A Contribution of Outstanding Value

With the renewed flow of books and periodicals, the return of volumes from their store, and the increase in the number of Fellows, space was once again the main preoccupation of the Council and librarians. The library began to spill over into corridors and committee-rooms as it had done previously, and the need for enlargement became pressingly urgent. Sir Henry Dale had been president of the Society during the years 1948–50 and was fully aware of these problems. On relinquishing office to Lord Webb-Johnson, he announced an offer from the trustees of Sir Henry Wellcome to provide a large sum of money for the extension of the library. This could be achieved by adding a fourth floor to the Society's house and altering the existing second floor so as almost to double the library space. At a Council meeting on October 17, 1950, the president reported the offer and expressed his deep appreciation of it. He called it "the most important matter which had been considered by the Council of the Society since 1907." The moment indeed was propitious, as Lord Webb-Johnson's experience in similar constructional enterprises was unrivalled. The result has been the addition of the fine Wellcome Research Library—a contribution of outstanding value to the progress of British medicine. For some years the librarians are, as a result of the most generous act in the history of the Society, again free from the recurrent anxiety about space.

TOBACCO A BLESSING?

"NO," SAY THE HUNTERIANS

"That tobacco is a blessing" was the proposition moved at a discussion meeting of the Hunterian Society at Apothecaries' Hall on November 16. After a number of speeches, serious and quizzical, the proposition "That tobacco is a blessing" was defeated, in an assembly of about 200 people, by a very large majority. The opener of the debate in favour of the motion was to have been Sir Alan Herbert, who was prevented by illness from attending. He sent a note in which he qualified his advocacy of tobacco by admitting that smoking was a barbarous practice and that a pipe was not really enjoyable until it was absolutely filthy.

Sir HENEAGE OGILVIE, President of the Society, who proposed the motion, said that he was ready to admit that cigarette smoking was a dirty, expensive, and psychopathic habit, likely to lead to cancer of the lung, duodenal ulcer, smoker's heart, and ash on the waistcoat. But the motion referred not to cigarettes but to tobacco, and who would say that tobacco was not a blessing? Wherever strong men went out into the wide open spaces of the earth they were accompanied by their pipes; statesmen smoking cigars presided over the councils of nations. It was smokers who had given us dominion over palm and pine, who had ensured that Britons never should be slaves. What was England before Raleigh? A downtrodden outpost of Europe. But after Raleigh how great she had become. The Dutch, the French, had failed to beat her. Napoleon and Hitler (a non-smoker, by the way) had gone down before her. "I do not feel that we can risk the great decadence that would be bound to come to a country which has no minor vices."

The Cost to the Community

Mr. DICKSON WRIGHT was the leading advocate on the other side. To him smoking in any form was anathema. A blessing? Perhaps so, to the man who indulged in it, but what of the community? The amount of tobacco consumed in a year would fill every cubic inch of space in St. Paul's Cathedral. The annual tobacco bill was £800 millions. A good smoker might consume half a hundredweight a year. He believed that many smokers secretly deplored their bondage to it. The habit was unattractive. He preferred the dignified figures of the past—the younger Pitt, Melbourne, Disraeli—to the pictures of their descendants, Baldwin with his pipe and Churchill with his cigar. On the stage how incongruous it would be to have Hamlet uttering his soliloquy pipe in mouth. What would Shakespeare have thought of a Noel Coward piece with smart sayings interrupted by cigarette puffs? He had counted the number of times cigarettes were lighted on the stage in modern plays—the record was 53 in a single play. In the auditorium the waning and waxing of interest in a play could be estimated by the manner in which the cigarettes glowed and smouldered out. He also complained of smoking by dignitaries of the Church. It was incongruous for a minister of the Gospel to allow himself to smoke whilst condemning lots of things of a more physiological nature. In private life he thought that ladies lost some of their charm by smoking. At no period of her life was a woman improved in appearance by a cigarette. It was a great triumph for the tobacco manufacturers when they overcame the delicacy of the female sex. It only remained for them to get the habit firmly established in the schools and then the home market would be fully saturated.

Smoking in the medical profession, Mr. Dickson Wright continued, was also a bad thing. The doctor whose clothes, breath, and fingers were malodorous from tobacco was a less good doctor. Nurses too—the question of smoking in uniform was exercising that matriarchal body, the General Nursing Council. At hospital the administrative staff, the porters, the cooks, the maids all smoked at their work. There seemed to be little restraint anywhere in the use of tobacco. It was not a blessing to the country; we should be much happier without it.

A Word in Defence

Dr. R. R. BOMFORD appeared as the chief supporter of the motion. He claimed only that this innocent herb had been a pleasure, a solace, and sometimes a delight to peaceful, well-adapted personalities for at least 400 years. He reminded the audience of the vast numbers of people employed in the tobacco industry, of the £600 millions or more that it produced in revenue, of the fact that it prevented thousands of people from getting fat, of the contribution it made to the serenity of the home, of the fact that a by-product was an excellent sheep dip. Much of the propaganda against it was irrational and prejudiced. In a recent controversy both cancer and smoking were subjects charged with emotion, so that it was not surprising that the combination led to outpourings of biased wrath. He had no quarrel with the work of Professor Bradford Hill and his associates, but it would be interesting to learn a little about the fate of male non-smokers. Did they retire to dark corners and die slowly from myocardial degeneration?

He complained of the term "addiction" as used in the case of tobacco. Smoking was a habit but not an addiction; there were no withdrawal symptoms. If people were to give up smoking because of the fear of dying from cancer of the lung they might as well give up bacon and eggs for breakfast, because this increased the coagulability of the blood and so made the partaker more liable to coronary thrombosis.

Smoking and Lung Carcinoma

Dr. HORACE JOULES, speaking with great earnestness, asked why, if tobacco was such a blessing, it was necessary to spend so many millions on persuading people to take up the habit. Of the dire results of smoking he pointed to the smokers' cough, which in the man who had been long addicted to a heavy daily consumption of cigarettes was not to be distinguished from the cough of lung cancer or advanced tuberculosis. Bronchitis was a curse of the community, and largely accounted for the fact that expectation of life of persons over 50 was little above the figure in the early part of this century. In 1950 16¼ million working days were lost by the insured population on account of chronic bronchitis. Tobacco was said to be a germicide, but in fact it prepared the bronchi for infection. Professor Bradford Hill's dispassionate study had not been refuted by any tobacco concern. Far more people were now dying of lung cancer than of pulmonary tuberculosis. There were three times as many deaths as from road accidents. Excessive smoking was hindering the surge forward in preventive medicine, particularly in respect of chest diseases. The difficulty was that the Treasury had a vested interest in this "blessing" to the tune of some £630 millions a year. He pointed to the vast amounts of tobacco imported which had to be paid for in dollars, while the allocation of cortisone was negligible by comparison. He begged his audience to experience the improvement in physical and mental well-being which would follow three months' abstinence.

As stated, the show of hands resulted in so large a majority against the proposition "That tobacco is a blessing" that the numbers were not counted.

Last year, according to the statutory Home Office return, over two million experiments on living animals were performed. The great majority of these (86%) involved no operative procedure, but simply inoculation, modification of the diet or environment, or administration of a drug or toxin. About 250,000 experiments were surgical operations under anaesthesia, many being of a minor character. Over half of all the experiments were made during the preparation, testing, and standardization of therapeutic substances; another 400,000 on behalf of Government departments and bodies such as the Medical and Agricultural Research Councils; 200,000 for public health purposes or directly for the diagnosis of disease, and 96,000 in the course of cancer investigations. Throughout the year 4,491 persons held Home Office licences, although apparently 1,335 licensees performed no experiments.

Reports of Societies

ACUTE LUNG INFECTIONS IN GENERAL PRACTICE

The subject of common acute lung infections in general practice was discussed by the General Practice Section of the Royal Society of Medicine on November 28.

Dr. JOHN FRY opened the discussion by defining the magnitude of the problem; 25% of all the patients he saw in his general practice were suffering from respiratory infections, and chest diseases accounted for 10% of all deaths. Acute pneumococcal pneumonia was a rarity in general practice, and textbook descriptions and classifications of the pneumonias were confusing and inadequate. Non-specific pneumonia without clinical signs of consolidation was common and received little mention in the books, and there was little agreement about the precise meaning of acute bronchitis; to some it meant merely productive cough with fever, to others the diagnosis required the presence of definite physical signs of abnormality.

Pneumonia was first classified on the basis of clinical description, then the morbid anatomists distinguished lobar and broncho-pneumonia, and most recently Dr. Scadding had emphasized the distinction between specific bacterial or viral pneumonias and the non-specific pneumonias, in which there was some abnormality in the respiratory tract predisposing to invasion by commensals. In general practice this classification was not altogether practical, since elaborate procedures were often required for precise bacteriological diagnosis.

A Clinical Classification

Dr. Fry said that in his own practice in South-east London he saw 60 to 80 patients with acute respiratory disease each year, mainly in the autumn and winter. He had found the highest incidence (135 per 1,000 at risk) in the over-70 and 5-to-9 age groups. He placed little reliance on pathological or radiological investigation and subdivided his cases into diffuse, with scattered and bilateral signs (53% of his cases), and local, with signs in one or more localized areas only. The second group were subdivided into those with (5%) and without (42%) clinical signs of consolidation. The diffuse infections had a sudden onset with cough and variable dyspnoea, and the physical signs included bilateral rales or rhonchi or both; these infections were either primary (no previous chest history) or secondary (previous chronic bronchitis, measles, or whooping-cough). The diffuse primary type occurred mainly in the under 10's and the diffuse secondary type in the over 40's. The cases with local signs of consolidation formed a small group (12 patients only); they usually responded to antibiotics.

Cases with local signs without clinical evidence of consolidation were very common in Dr. Fry's practice, but were scarcely mentioned in standard books. They were mild infections occurring at all ages, but especially in children, and rapidly resolved. The onset was insidious, though there was often a preceding nasal discharge; the systemic disturbance was variable, and the patients often remained ambulant with little or no fever or tachycardia. There might be an irritating cough, or chest pain, and at one or other base there was an area of diminished air entry, maybe impaired percussion note, and a shower of inspiratory rales. There was disappointing correlation of the radiological appearances with the clinical signs. The erythrocyte sedimentation rate and white-cell count were usually normal, specific pathogens in the sputum were not found, and in only a very few patients were virus complement fixation tests positive. The condition might be caused by a primary low-grade infection, or by mechanical aspiration bronchial embolism producing segmental or lobular collapse, with secondary infection. Treatment consisted in control of the infection, when necessary, and postural drainage with breathing exercises to overcome the mechanical factors.

Dr. Fry concluded by asking a number of questions, for which answers had still to be found. What, he asked, was the relative importance of mechanical embolism, allergy, and degeneration; what was the influence of season and climate; what was the relation of chronic bronchitis and influenza to the acute chest; and what part did fog play?

Aetiological Factors

Dr. J. G. SCADDING said that a classification, to be logical, must be on the same basis—for example, aetiological—throughout. With the pneumonias this was impossible, because there were still unidentified aetiological agents, and present knowledge was often difficult to apply in actual practice. Furthermore, not every infection had only one aetiological agent, and often mechanical factors played a part. He referred, in this connexion, to the series of cases described by Ramsay and himself in 1939; these patients were suffering from acute upper respiratory infections or chronic bronchitis with an acute flare-up, and were found to have localized opacities in the radiograph. This was attributed to aspiration of mucus infected with upper-respiratory-tract commensals with resulting obstruction of a bronchus, notably in the posterior segments when the patient was recumbent. This was followed by absorption of the alveolar air and a mild pneumonic reaction.

Dr. Scadding then outlined his own classification of the pneumonias. There were two main groups: *Specific infections:* (*a*) bacterial (pneumococcal pneumonia was still common in hospital practice); (*b*) viral (of which the psittacosis–ornithosis group was the only named one, though there certainly were other unidentified pneumotropic viruses causing what was still sometimes known as primary atypical pneumonia); (*c*) associated with viruses (notably with measles and influenza) and due to the combined action of virus and bacteria; and (*d*) rickettsial (Q-fever) and other rarer infections. *Aspiration pneumonias:* (*a*) diffuse—that is, bronchopneumonia—including post-operative, deglutition, terminal, hypostatic, and inhalation pneumonias; (*b*) localized; and (*c*) suppurative pneumonia. He related two typical case histories to illustrate the differences between virus pneumonia and aspiration pneumonia. The patient with virus pneumonia, in contrast to the one with aspiration pneumonia, had severe constitutional disturbance, with only minimal respiratory symptoms.

Aetiological diagnosis, in Dr. Scadding's opinion, was difficult. Bacteriological examination of the sputum was hampered by irregular distribution of pathogens in the sample. Serological diagnosis was dependent on the demonstration in a rising titre of specific antibodies or cold agglutinins, and could often be made only retrospectively. Treatment must be started without a precise diagnosis, and Dr. Scadding referred to a previously published study undertaken in 1950 in which the results of treatment of clinical pneumonia by standard methods—penicillin or sulphonamides—were compared with treatment by aureomycin and by chloramphenicol. In this trial the standard treatment was at least as effective as the newer antibacterial agents, was accompanied by fewer side-effects, and was much cheaper.

Radiological Diagnosis

Dr. PETER KERLEY showed an interesting series of radiographs illustrating the radiological features of different types of pneumonia. In pneumococcal pneumonia the opacity spread out from the hilum, and when the whole lobe was consolidated its bulk was usually increased. Increase in the bulk of a lobe or a segment was a feature of all bacterial pneumonias, while interstitial changes predominated in the virus diseases unless there was secondary infection. Pseudo-cavities due to acute vesicular emphysema were common during resolution in children. Delayed resolution and atelectasis were rare, but might be followed by bronchiectasis. Tuberculous pneumonia, measles pneumonia, and virus pneumonias (sometimes involving multiple segments) associated with upper respiratory infections were also illustrated.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Sterilizing Ampoules

SIR,—Your issue of November 21 (p. 1165) reports an action for damages brought by two patients in whom spinal anaesthesia was followed by paraplegia. This was said to have resulted from contamination of the anaesthetic by phenol, in a solution of which the ampoules had been stored.

I wish to suggest that the antiquated practice of storing ampoules, whether of such solutions, of catgut, or any other material, in disinfectant solutions, or even of "dishing them up" in such solutions, should be altogether abandoned. The surface of these ampoules, if the surgeon is to open them, must of course be sterile, but this can be ensured in more convenient and less dangerous ways, apart from the use of heat, which is applicable to some of them. There are two obvious possibilities: (1) that they be sterilized by the manufacturer, and protected against contamination before use by covering with "cellophane" or enclosure in an outer glass tube; and (2) that they be sterilized chemically by the user, but after immersion for a sufficient time in a suitable solution they should be transferred to sterile distilled water to free them of the disinfectant, and then stored in an air-tight container until required. It does not seem to be generally understood that once an object has been sterilized it can be kept so indefinitely, or as near sterile as does not matter, merely by protection from atmospheric dust. An easy way of ensuring this is to place the ampoule in a plugged sterile test-tube. If something more elaborate and commodious is wanted, it should not be beyond modern engineering skill to construct a cabinet, itself sterilizable, which would accommodate numbers of such ampoules under conditions affording complete safety.

If it is a fact that solutions can traverse the apparently intact walls of these ampoules, it would be a wise precaution to colour the disinfectant solution strongly so that the results of this process can be seen. A suitable disinfectant would be liq. formaldehydi chirurgicalis acting for six hours: this will kill anything, including spores, which phenol will not.—I am, etc.,

London, E.C.1. LAWRENCE P. GARROD.

Amoeboma of the Caecum

SIR,—In his memorandum (*Journal*, November 14, p. 1087) Mr. E. N. Callum tells a sad story which might well have had an even sadder ending. While Mr. Callum gives us details of his surgical interference, there are many other things that he does not tell us. For example, he says that the patient was a clerk of 34 years, but he does not tell us where he spent those 34 years. Since an amoeboma does not grow in three days, it would have been interesting to know what earlier symptoms the patient had had, or, in the complete absence of any symptom, an assurance of this fact. He states that, on the original diagnosis of appendix abscess being made, antibiotics were given, but he does not tell us which antibiotics and especially whether they included aureomycin, for example, for which amoebicidal properties are claimed. One would like to know what the pathologist thought about the supposed neoplasm during the three weeks between the operation and the sloughing of the abdominal wall; in fact, we are never told what the pathologist did eventually conclude about the tumour, and we have only the title of the paper to suggest that it was an amoeboma. Had it been a neoplasm combined with an *Entamoeba histolytica* bowel infection, the immediate result might well have been the same.

Mr. Callum's comment is both wise, in that he gives the excellent advice that when doubtful masses are found in the bowel amoebiasis should be excluded, and laudable, in that he risks personal criticism to ensure that others do not fall into the same error—but he does not go far enough. In his last sentence he writes: ". . . while the presence of unusual masses in the rectum or elsewhere in the bowel may call for a search for *Entamoeba histolytica* in the stools before proceeding to surgery." Does he mean one or two hurried stool examinations by the hospital technician, who will rarely be experienced in identifying *Entamoeba histolytica*? If so, surely the procedure would be valueless to *exclude* amoeboma. Even a dozen such examinations by an experienced parasitologist would be inadequate and would take time that could be much better spent in the carrying out of an adequate therapeutic test with emetine.

This case report exemplifies the timeliness of the memorandum presented by the council of the Royal Society of Tropical Medicine and Hygiene at the recent World Conference on Medical Education; two of its main points were that all students should be taught to include in their case histories the past geographical movements of patients, and that their courses of instruction should at least include a few lectures on tropical medical and surgical emergencies that are likely to be encountered in non-tropical countries.—I am, etc.,

London, W.1. L. EVERARD NAPIER.

Malaria in Ex-Servicemen

SIR,—Sir Neil Hamilton Fairley, in his letter about "Malaria in Ex-Servicemen" (*Journal*, November 21, p. 1157), states: "Outside the armed Forces and the various hospitals for tropical diseases, many patients with vivax malaria *only* receive treatment with schizonticidal drugs . . ." (my italics). He goes on to recommend, apparently in all cases, a course of one of the 8-aminoquinoline drugs.

In the Refresher Course article on malaria (*Journal*, October 27, 1951, p. 1021), Sir Gordon Covell writes: "The routine administration of (the 8-aminoquinolines) in all cases of vivax malaria is not recommended. They should be reserved for the treatment of stubbornly relapsing cases, more especially in circumstances where there is no risk of reinfection."

As the vast majority of the cases of vivax malaria in ex-Servicemen, at least in those returning from Korea, do not fall into the category of "stubbornly relapsing," it would be of interest to know why these eminent authorities differ.—I am, etc.,

Glasgow. I. B. MUNRO.

SIR,—The attention recently given to relapsing malaria in the medical press is most timely. I venture to suggest that the huge majority of medical men are nevertheless left without the faintest idea of the optimum treatment for this condition. I have found that a number of practitioners in this neighbourhood have been grateful for some forthright guidance in this matter, with consequent benefit to their ex-Service patients. I therefore feel that practitioners would warmly welcome a simple directive from the Ministry giving clear-cut advice on the therapy of malaria. One has only to question patients admitted for malaria to discover the urgent need for such authoritative guidance.

The corollary to this is the great research opportunity that is being lost through lack of any standardizing of treatment. The arguments in favour of self-determination in prescribing are irrevelant when applied to the treatment of tropical diseases in temperate climates.

There is one other point I should like to stress. Far too little prominence is given to one of the great cardinal signs of malaria—namely, vomiting. In any ex-Servicemen from Korea suffering from pyrexia and vomiting without physical signs, malaria should be thought of first.—I am, etc.,

Worcester. C. F. J. CROPPER.

Histoplasmosis in Great Britain

SIR,—The lack of clarity in our paper must have been due to its brevity. We meant to infer that the cases described, including that of Duncan,[1] did not conform to the criteria accepted for *Histoplasma capsulatum*. This in fact has been accepted by Duncan himself in his letter (*Journal*, November 14, p. 1103).

To correct and amplify the statement made in the latter part of his letter I should point out that we now have information to the effect that, including the case described by us, five cases of disseminated histoplasmosis have occurred in Great Britain, and two cases showing the local manifestations without apparent dissemination (including the case described by Duncan in 1947) have also been reported, making seven cases in all. Of these five cases of disseminated histoplasmosis, one was diagnosed during the patient's lifetime (the case we described), another was suspected during the patient's lifetime but confirmed on necropsy. The three other cases were only diagnosed at necropsy. Of this group of five cases, four gave positive cultures of *Histoplasma capsulatum*, whereas the fifth did not, the organism in this case only being identified in stained sections of the tissues. Of the two cases presenting with local lesions, the case described by Duncan gave a positive culture which was not typical of *Histoplasma capsulatum*, but probably due to related species now given the name of *Histoplasma duboisii*. Positive culture was not obtained from the other case.

It is extremely difficult to know whether it is justifiable to distinguish the clinical manifestations of the condition due to *Histoplasma capsulatum* from that due to related species, but there would appear to be some evidence at least to suggest that the disseminated histoplasmosis as classically described is invariably due to the typical *Histoplasma capsulatum*.—I am, etc.,

Romford, Essex. S. LOCKET.

REFERENCE

1 *Trans. roy. Soc. trop. Med. Hyg.*, 1947, **40**, 364.

Control of Tachycardia by Quinine

SIR,—With reference to Dr. C. W. F. Winckel's letter (*Journal*, November 14, p. 1103), Wenckebach was not the first to discover the beneficial effect of quinine in some heart disorders. Pride of place goes to Senac, who published an account of quinine being used in such circumstances in the year 1749.[1] Wenckebach merely followed up a chance observation of one of his patients who was taking quinine, and discovered that it was exerting an effect on the heart rate.—I am, etc.,

Collingborne Ducis. B. H. BASS.

REFERENCE

1 *Traité de la Structure du Cœur, de Son Action et de Ses Maladies*. 1749. Vol. 2, p. 526. J. Vincent, Paris.

Cough Syncope

SIR,—Professor E. P. Sharpey-Schafer (*Journal*, October 17, p. 860) describes the physiological mechanism of syncope after coughing. The syncope from coughing was shown to be due to vasodilatation following stimulation of baroceptors by large arterial cough transients. It is interesting to note how this syncope can be induced by stimulating the carotid sinus reflexes,[1] and one feels that in syncope after coughing this particular reflex plays a large part. Watching these patients, who are usually short-necked people, coughing, one observes the tendency to raise the shoulders and tighten the neck muscles.

I am of the opinion that these patients who lose consciousness, and all who cough violently and thus induce different degrees of dizziness, should be taught to cough differently. As soon as the patient feels "the upper respiratory tickle" he should bend slightly forward, pushing his chin forward and stretching the neck muscles. I do not know if this manœuvre protects the carotid sinus, reducing the stimuli to the receptors there, or if the varying of the stance adopted reduces the violence of the cough. Professor Sharpey-Schafer points out that when coughing is associated with expectoration there is no syncope, and the usual posture adopted when bringing up phlegm is one with the neck extended.

During the last two years I have had three cases of syncope after coughing. One was a doctor, aged 48, who had not smoked for four years because it made him cough so much. He had a fit of coughing when sitting playing bridge, and this was followed by an attack of syncope with slight convulsions. Another was an accountant aged 38—a heavy smoker. He fell in the street following a coughing bout. I had previously warned this man of the possibility of syncope, because I had seen him coughing. A third case was that of a man aged 80, a heavy smoker, who had a coughing bout in a train and fell on the carriage floor. Each of these three men could be described as being short-necked. Only the second patient wore tight neckwear.

The first and second patients had had no previous attacks, but the third had had them on a number of occasions and was afraid to consult a doctor, believing he was suffering from some strange malady. It is possible that in the case of this elderly man he was prone to frequent attacks because of atheromatous changes in the blood vessels causing increased hyperactivity of the vagal reflex arc.[2] None of these three patients have had any attacks of syncope since they have adopted the posture that I have described.

It would be interesting if one could ascertain the difference in the intrathoracic pressure in a patient coughing with his shoulders shrugged, and coughing with his neck extended.—I am, etc.,

Hove. S. CALLER.

REFERENCES

1 Evans, E. (1952). *J. Amer. med. Ass.*, **149**, 46.
2 Judson, W. E. (1953). *Med. Clin. N. Amer.*, **37**, 1313.

Treatment of Plantar Warts

SIR,—Every day I am confronted with warts plantar, warts palmar, warts digitate, warts acuminate, warts plane, and warts vulgar, and they never cease to rouse my spleen because they are there, because their possessors demand their instant removal, and because this puts me to so much unnecessary trouble and expense of time. For I know that I do not know very much about warts; and yet I know enough about their ways to know that they have the laugh of me—they, and the owners of the gift of charming. Whereas I have to bring a whole armoury to bear, curettes, cylinders of carbon dioxide, containers of liquid nitrogen, red-hot wires, *x*-ray tubes, and the like, the charmers blithely pronounce the warts cured and behold they vanish—sometimes, but sufficiently often to impress. Those people who believe that such things only happen to the simple-minded in the depths of the country should read of what befell Sir Francis Bacon in Paris in the year 1576, as recorded by Walter de la Mare (on p. 690) in his delightful anthology *Come Hither*. To those who feel that there is more virtue in numbers and a planned experiment I recommend an article by Bruno Bloch.[1] There is no doubt about it, the charmers and we are armed like David and Goliath. And their mystification at their success is not the least galling part of the matter. And so, Sir, beset as I am by these verrucosities which I detest and which are a daily reproach to me, I have been goaded into writing to you by the telling shafts of your annotator on plantar warts (*Journal*, November 14, p. 1093), who has no doubts about our ignorance of this subject. My observations do not go very far, but they might form a stepping-stone for others.

There are at least two kinds of plantar wart. One is painful and penetrates the skin deeply. It can be curetted out most satisfactorily, and when this is done leaves a deep, round hole with an overhanging rim of stratum corneum. The other kind is a dry, crumbling affair, causes little pain, and is superficially placed in the skin. Curettage of this kind discloses the wart as a plaque of tissue compounded of hundreds of small warts. The hole left by this second kind is a shallow thing, polycyclic in outline. The natural history of each kind after curettage varies, for whereas the former is usually cured the latter usually reforms. The resistance of the latter kind to curettage is typical of its behaviour with every kind of treatment, and so is the

willingness of the former to disappear. These two kinds of wart are well known as "the plantar wart" and "the mosaic wart."

Thus far there is nothing new, but Dr. J. A. R. Miles and I discovered[2] that the clinical distinction was also histological. The bulky plantar wart contained eosinophilic inclusion bodies, both intracytoplasmic and intranuclear. The mosaic wart did not. This plantar wart which contained inclusion bodies we proposed to call a myrmecia for historical reasons.[3] The myrmecia, we found, occurred on the hands occasionally, where it preserved its clinical characteristics, except for a greater projection above the surface on account of the absence of pressure. The common wart of the hands was devoid of inclusion bodies, and where a patient had warty hands and feet myrmecia would pair with myrmecia, and common wart with mosaic wart. In a transmission experiment the myrmecia extract gave rise to a myrmecia and the common wart extract to common warts. Finally, Strauss and others in America,[3,4] working independently, claimed to have photographed wart virus under the electron microscope. They found the virus in some warts but not others, and it seemed to me from their description that the warts which produced virus were identical with our myrmecia.

Nothing which I have seen since we wrote our article has made me want to alter our conclusions.—I am, etc.,

Edinburgh, 12. ALAN LYELL.

REFERENCES

1 *Klin. Wschr.*, 1927, **6**, 2271 and 2320.
2 *British Medical Journal*, 1951, **1**, 912.
3 *J. invest. Derm.*, 1950, **15**, 433.
4 *Proc. Soc. exp. Biol. (N.Y.)*, 1949, **72**, 46.

SIR,—Your annotation (*Journal*, November 14, p. 1093) prompts me to suggest a simpler method of treating plantar warts than those described. This method was described by Dr. W. Gillies Annan[1] and consists in injecting a 5% aqueous solution of phenol through normal skin at the edge of the wart into its base. The prick is painless, but the actual injection is very painful for a few seconds. The patient, however, walks away painlessly and cured, for the wart disappears in a few weeks.

I have dealt with dozens in this way without a failure. I always warn the patient—usually a school-child—that the injection will be painful for a moment, but with explanation this prospect is usually accepted when weighed against the continual pain of walking on a wart: and most children are quite ready to be brave.

My only modification of Dr. Annan's method is to use less fluid than he suggested. I find that 1–3 min. (0.06–0.18 ml.) is usually sufficient. He recommended 5–10 min. (0.3–0.6 ml.). The method is speedy, apparently safe, and sure.—I am, etc.,

Reading. P. M. R. HEMPHILL.

REFERENCE

1 *Lancet*, 1948, **1**, 926.

Routine Lumbar Puncture in Primary Tuberculosis

SIR,—This problem, mentioned in "Any Questions" (*Journal*, November 7, p. 1058), was well illustrated by a boy aged 2 who was admittted under my care last March with an acute tonsillitis and meningism. Lumbar puncture produced a normal C.S.F. He became afebrile on the third day, but the temperature began to rise on the fifth day and meningism developed again, so that a further lumbar puncture was carried out, and this showed all the changes of tuberculous meningitis.

The boy was in contact with his grandfather and had been under regular observation for tuberculosis for some time. One year previous to admission the Mantoux 1/100 was positive, so that he had evidently been infected at least a year prior to admission. It is possible that the acute infection precipitated the tuberculous meningitis, but it seemed to me more likely that the lumbar puncture had done so.

The boy's further history is of interest, as he developed poliomyelitis whilst still under treatment, but the paralysis was limited to the left upper arm which has never been injected, though he was receiving daily intramuscular streptomycin injections into each thigh before, during, and after the superadded virus infection occurred.—I am, etc.,

London, N.18. IAN G. WICKES.

Lumbar Puncture

SIR,—Dr. William Gooddy, in his article on lumbar puncture (*Journal*, November 7, p. 1040), made no mention of the lateral approach. If the needle is inserted an inch (2.5 cm.) from the midline the tough intraspinous ligament is avoided and the progress of the point of the needle through the dura is more readily detected by the fingers. Very little practice is required to estimate correctly the angle that the needle must make to the median sagittal plane.—I am, etc.,

Hove. REX BINNING.

SIR,—I was interested in the article by Dr. W. Gooddy on lumbar puncture (*Journal*, November 7, p. 1040), which, I gather, was only a preliminary article in a series. There are, however, two questions I would like answered: (1) should a lumbar puncture ever be performed in the home, and (2) if so, when?—I am, etc.,

Petworth, Sussex. W. A. BALL.

Milk and Protozoal Infections

SIR,—The publication of Professor B. G. Maegraith's letter (*Journal*, November 7, p. 1047) stimulates me to record the following facts that have recently come to hand through the kindness of Miss L. M. Fagg, nursing sister at the Baptist Mission Hospital, Yakusu, Belgian Congo. We were interested in the suggestion made in the article by Professor Maegraith, Mr. T. Deegan, and Dr. E. Sherwood Jones (*Journal*, December 27, 1952, p. 1382) that a positive suppressive effect of milk might explain the low incidence of malaria in infants wholly breast-fed, and the further suggestion of Dr. F. Hawking (*Journal*, May 30, p. 1201) that the suppression of malaria in the experimental animal raised on a milk diet might be due to the negligible amounts of *p*-aminobenzoic acid in milk.

During a short period, ten of eleven children under the age of 6 months admitted as in-patients to the Yakusu Hospital had ring-forms of *P. falciparum* present in the thick drop. None of these infants had received any food whatsoever but their mother's milk. Investigations are being continued to discover if other factors are involved.—I am, etc.,

London, S.E.9. S. G. BROWNE.

Treatment of Tetanus

SIR,—The recent correspondence (*Journal*, November 14, p. 1099) on the prognosis and treatment of tetanus gives the impression that modern treatment rests entirely on the use of the newer relaxants, antitoxin, intubation or tracheotomy, and controlled respiration. No reference is made to surgical excision of the site of infection, but surely the question of whether or not this has been, or can be, carried out is of primary importance in prognosis; other forms of treatment cannot be fully effective if toxin is still being produced at the site of infection.

In 1944, while working with a medical team of the Friends' Ambulance Unit in a very remote part of South-west China, a case of fairly severe tetanus under my care recovered without any adjuvant treatment beyond morphine, chloral, and bromide. No antitetanic serum was available at that time. The site of origin was a septic pulp wound of the right thumb sustained three weeks previously, and symptoms had been present for 10 days at least. The terminal phalanx was amputated immediately, and over two weeks elapsed before the spasms started to abate. I feel sure that recovery was only possible because of the complete extirpation of the site of origin of toxin.

It is to be hoped that recent medical advances in the treatment of tetanus will not obscure the essentially surgical pathology and treatment of the disease.—I am, etc.,

Diss. PATRICK D. RAWLENCE.

Cancer and the Public

SIR,—Dr. James Brailsford (*Journal*, November 14, p. 1104) is still attempting to spread alarm and despondency among the surgeons who deal with cancer. He has in other letters said, "We have no cure." Certainly no surgeon confronted by a patient with a small, hard, non-fluctuating lump in her breast would promise her relations that she could be cured. But the results of skilful and bold surgery are well worth while. There are different grades of malignancy, and some cases of cancer are hopeless from the start; even at the time of diagnosis the growth has already caused metastases by spread through arteries or lymphatics. Professor McKinnon, of Toronto University, who displays some large and depressing statistics, thinks that the breast cases who live for very many years after the operation are not properly malignant.[1] But this is the opinion only of a distinguished man; he cannot prove it and we need not believe it. Certainly I know women who are well 25 years after removal of breasts that were proved by pathologists to be cancerous. The word "cure" is applicable there.

A large proportion of those in whom the trouble "recurs" after six or seven years have had excellent health in the meantime. It is absolutely wrong to say that untreated women with cancer who live for some time are free from pain, mental misery, or ulceration. Simple mastectomy was much practised by country surgeons 60 years ago; the results were appalling and gave surgery a bad name—operations must be thorough.

Human adult life is not a very long affair, and if surgeons can in a certain proportion of their cases, give a middle-aged woman 5, 10 or even 15 years of cheerful life before the onset of old age (in which she is certain to be afflicted in many ways) they have done very well for her. Claudio said (in *Measure for Measure*): "The miserable have no other medicine but only hope. Let not Dr. Brailsford try to take this away.—I am, etc.,

Hastings. HARRY GABB.

REFERENCE

[1] *Canad. J. publ. Hlth*, 1949, **40**, 257.

Public Health Laboratory Service

SIR,—While I would agree entirely with Dr. M. T. Parker's opinion (*Journal*, November 7, p. 1048) that close co-operation between the hospital and public health services is essential, and that the form that it takes should depend upon local circumstances, I regard his original description of the function of the Public Health Laboratory Service (*Journal*, October 10, p. 823) as wholly misleading.

Unless there is to be an absurd degree of duplication of resources, I would suggest that the work of the Public Health Laboratory Service should properly be confined to the investigation of *established* outbreaks of infectious disease, and the routine bacteriological control of water, milk, food, and other environmental factors. General practitioners are now making an increasing use of the facilities offered by the local hospital laboratory, where the haematological, bacteriological, biochemical, and histological aspects of any case can be considered side by side, to the great advantage of the patient. Moreover, the local hospital bacteriologist can offer a diagnostic service at least as efficient as that at the area public health laboratory. Any tests which may be of a particularly specialized nature can be, and often are, referred direct to the appropriate central reference laboratory.

Most of Dr. Parker's article would serve very well as a description of the services already available to general practitioners at the local hospital laboratory. The investigation of some of the illnesses listed would seem to be quite outside the province of the Public Health Laboratory Service, which is fundamentally a bacteriological service. For example, it appears that blood is going to be examined for evidence of glandular fever. Most haematologists would agree that neither a negative nor a positive Paul–Bunnell test should be accepted without a total and a differential white cell count. Such contact as I have had with junior bacteriologists under training for the Public Health Laboratory Service has made it clear that the study of haematology plays no significant part in their curriculum. Dr. Parker's article has important implications, and it should be made clear whether the opinions he expressed are to be regarded as the considered policy of the Public Health Laboratory Service.—I am, etc.,

Chertsey, Surrey. ROBERT J. EVANS.

Site for Vaccination

SIR,—I read with interest Dr. J. Cantor's letter about the vaccination on the sole of the foot (*Journal*, November 7, p. 1050). I had myself only seen and performed vaccination on the arm or thigh, and was surprised when the local general practitioner here vaccinated my daughter just lateral to the second lumbar vertebra. He said he invariably used this site, and claimed almost 100% "takes." This site still allows the baby to be bathed in shallow water, is usually free from faecal and urinary contamination, and it will be concealed by bathing costume or evening dress in later life.

The only disadvantage I can see with the sole of the foot is that if the child is vaccinated or re-vaccinated when she is several months old it will be painful when crawling or walking, and she can easily pull the dressing off—neither factor applying to vaccination at the lumbar site.—I am, etc.,

Ghent, Belgium. DOROTHY M. ROELS.

SIR,—I was interested to read Dr. J. Cantor's reference to the sole of the foot as a vaccination site (*Journal*, November 7, p. 1050). Six years ago it occurred to me that this would have the advantages that Dr. Cantor has pointed out, and I started using this site then, and always do so now in the case of female infants, except when the mother does not wish it. The only way in which my experience seems to differ from that of Dr. Cantor is that I do not find the percentage of "takes" quite so high on the sole of the foot, as, for instance, on the arm.—I am, etc.,

Canterbury. PATRICK OSBORNE.

Orthopaedic Care in Poliomyelitis

SIR,—Dr. Hugh Garland and Mr. J. M. P. Clark (*Journal*, November 14, p. 1105) appear to apportion blame equally to "senior members of our profession" for "bickering in public," but Sir Reginald Watson-Jones, President of the British Orthopaedic Association, was doing no more than his duty in pointing out to the Welsh Regional Board the omission of an orthopaedic surgeon in their panel for research in acute anterior poliomyelitis. The Leeds region is to be congratulated for following for the past six years the usually accepted pattern of treatment for this disease.—I am, etc.,

Norwich. H. A. BRITTAIN.

Piperazine in the Treatment of Threadworms

SIR,—Following the publication of our report on a clinical trial (*Journal*, October 3, p. 755) the subsequent wide use of piperazine hydrate in the treatment of threadworms has elicited reports of side-effects not in accordance with our experience. In relation to the very considerable number of cases treated in general practice these reports are few, side-effects having been recorded in 14 adults and 6 children. Nevertheless, we consider them worthy of attention. The manifestations are similar in all cases, notably giddiness and lack of co-ordination resulting in dropping things. Sickness, inability to focus vision, and a sense of detachment have also been noted. These effects have, for the most part, been mild and recovery has been rapid.

Predominantly, these side-effects have occurred in adults and may be associated with wide variations in weight of the patients and with variation in capacity of the domestic tablespoon as a unit of measure. Also, the piperazine hydrate is embodied in a heavy syrup vehicle which forms a high meniscus when the spoon is completely filled. It is thought that these three factors have occasionally resulted in dosage considerably in excess of the

recommended 50–75 mg./kg. The variation in the domestic tablespoon was investigated by measuring the capacity of nine spoons drawn from different households. Each spoon was filled level with water and also to its maximum with the heavy piperazine syrup. While the variation in capacity of tablespoons is notorious, the findings listed below are of interest:

Spoon No.	Filling Level with Water	Overfilling to Maximum with Piperazine Hydrate Syrup
1	5 drachms	8 drachms
2	6 „	8 „ 40 min.
3	4 „ 20 min.	6 „ 10 „
4	6 „	9 „ 20 „
5	6 „	9 „ 50 „
6	5 „ 40 „	9 „ 20 „
7	6 „ 40 „	9 „ 25 „
8	6 „ 10 „	8 „ 40 „
9	5 „ 20 „	8 „ 10 „

Note: 1 drachm = 3·5 ml. 60 minims = 1 drachm.

These can be summarized as follows: Of the nine tablespoons filled level with water one held ½ fl. oz. (14.2 ml.), two held 25% excess, and six held 50% excess. Of the nine tablespoons filled to the maximum with piperazine hydrate syrup, eight held 100% excess or more, and one held 50% excess. To take the worst example, it will be observed that in spoon No. 5 the dose of syrup may reach nearly two and a half times the intended 4 drachms.

It is recommended that, in the use of this drug, account must be taken of variation in weight of the patient, and that for the treatment of adults the prescribed quantity should be measured in a graduated medicine glass.—We are, etc.,

R. H. R. WHITE.
O. D. STANDEN.

London, N.W.1.

Sweating in Shock

SIR,—In the *Journal* of October 10 (p. 832) Dr. Ronald Woolmer suggested that some other explanation than sympathetic overactivity was needed for sweating during shock or surgical operations. Experiments carried out by Dr. T. S. Lee and myself[1] have suggested that sweating accompanies extensive central nervous activity of various kinds and that the sweat glands of the axillae, palms, and soles sweat most readily in response to such central nervous causes. Mild sympathetic excitation *per se* does not give rise to sweating.

Although it is undesirable to seek teleological explanations for all phenomena, Dr. Woolmer's request for such an explanation can be met in this case. Extensive central nervous activity in primitive man is most likely to have resulted from fear, anger, hunger, love, or injury, and in all these circumstances recognition of friend or foe is important. Since sweating in the axillae has the strongest smell and since sweating of the soles, and to some extent also of the hands, will leave the most scent in the tracks, it seems teleologically sound that those regions should sweat the most readily in response to central nervous stimuli. Sweating of the hands may also help grasping.—I am, etc.,

E. M. GLASER.

Singapore.

REFERENCE

1 *J. Physiol. (Lond.)*, 1953, **122**, 59.

Single-sample Test in Differential Diagnosis of Jaundice

SIR,—The evidence presented by Dr. Ian Wang (*Journal*, October 31, p. 971) for the inclusion of cholesterol determination in single-sample liver-function tests is undoubtedly convincing, but is liable to be received unfavourably by our already overburdened laboratories. However, there is a simple substitute in the form of the lipid turbidity test described by Kunkel *et al.*[1] which, although indicating changes in the total lipids (which is very often influenced by the phospholipid fraction), appears to parallel very closely the cholesterol content of serum.

The reagent and technique are extremely simple and require a minimum of working time: 1% liquid phenol in 12% NaCl in distilled water is kept in the refrigerator and 0.2 ml. of serum is mixed with 6 ml. of this phenol/saline solution. After standing for 30 minutes, the mixture is shaken and read as in the case of thymol turbidity. The units are calculated by assigning an arbitrary value of 15 units to a suspension of $BaSO_4$ (3 ml. of 1.15 g. $BaCl_2.2H_2O$ in 100 ml. water made up to 100 ml. with 0.2N H_2SO_4), which is read as a standard. My own range of normal variation is about 2 to 10 units, but it is a wise procedure for each laboratory to determine its own normal limits. I have used this test for a number of years, and, in addition to Dr. Wang's interpretations, have found it of value in distinguishing between acute and chronic hepatitis, since the former gives high normal or even elevated values, while the onset of cirrhosis is usually accompanied by low values. Indeed, a value below 2 units is of grave prognostic import. High values are found in fatty liver due to alcoholism when often the only abnormality is a raised lipid, while in biliary cirrhosis associated with xanthomatosis very high figures are encountered.

A valuable feature of this lipid test is that it enables one to eliminate false positive thymol turbidities which sometimes (though not always) occur in the presence of a raised lipid. In a recent paper dealing with liver function tests in myeloma, Dr. L. L. Griffiths[2] found difficulty in correlating some of his positive thymol turbidities with results obtained by other workers in this field. I feel these anomalous positive results are false reactions due to excessive lipid, particularly as Dr. Griffiths's excellent electrophoresis figures show an increase in β globulin in the sera in question and it is now fairly well established that lipid forms a complex with β globulin.

Before using the lipid test, I used to check the thymol turbidity by putting up 0.3 ml. of serum in 7.5 ml. 15% alcohol, which Mawson and I[3] found to give almost identical turbidities to those obtained in the thymol test. However, I still carry out this alcohol turbidity test in order to have, together with the lipid reaction, a double check on the thymol reading.—I am, etc.,

E. B. LOVE.

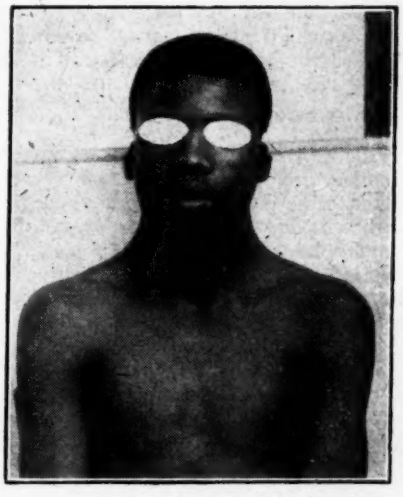
Preston.

REFERENCES

1 *Gastroenterology*, 1948, **11**, 499.
2 *J. clin. Path.*, 1953, **6**, 189.
3 *Lancet*, 1948, **2**, 850.

Turner's Syndrome in the Male

SIR,—The accompanying photograph was taken within three weeks of my reading the article by Drs. R. Sougin-Mibashan and W. P. U. Jackson on Turner's syndrome in the male (*Journal*, August 15, p. 371). The subject is a Zulu youth who had but recently arrived in Durban to seek work. By statutory regulation all such persons have to undergo a medical examination before they can be employed, and as a medical officer to the Native Administration Department about 120,000 go through my hands each year. This is the first case remotely resembling the Turner syndrome that I have seen during the past seven years.



Age 19 years, height 5 ft. 1 in., well built and muscular with a masculine voice, masculine distribution of body hair, a larger than average penis, but testicles small and firm. In addition to the webbing of the neck, the photograph distinctly shows congenital malformation in both ears. Mentally he was bright and gave a good account of himself. He disavowed interest in sex, and never had an erection.

He promised to return for further investigation, but this now seems unlikely. I gather from my staff that he looked upon my activities toward himself as a form of witchcraft, and it was obvious that he was anxious to be off.—I am, etc.,

D. F. MACKENZIE.

Durban.

Nocturnal Myoclonus

SIR,—In regard to your annotation (*Journal*, November 21, p. 1148) on nocturnal myoclonus, I should like to ask whether all the discussion on what has been termed "Ekbom's syndrome" since 1944[1 2] does not refer to the same subject as that of your annotation. If so, the general opinion seems to have been that the syndrome, sometimes familial in nature, is not definitely related to epilepsy.

Surely the tendency for the myoclonic jerks to appear on going to sleep may be compared to the occasional so-called "hypnagogic apparitions," the myoclonic jerks being due to the lowering of cortical control on going to sleep, and the hypnagogic apparitions being due to the commencing of dreams before brain unconsciousness has been fully established. I think this was an old view entertained before discussion on the subject was resuscitated by the writings of Ekbom and others. I should like also, if possible, to hear whether during the nocturnal myoclonus periods the knee-jerk responses are of the trepidation type.—I am, etc.,

London, N.W.1. F. PARKES WEBER.

REFERENCES

1 Ekbom, K. A. (1944). *Acta med. scand.*, **118**, 197.
2 Ibid., 1945, Suppl. 158.

SIR,—Last May the *Journal* contained a description of proctalgia fugax wherein a hint was given that the condition was an epileptic variant (*Journal*, May 16, p. 1083), and a subsequent correspondent (*Journal*, July 25, p. 224) effectively dealt with this concept by describing his ability to abort this manifestation, including the vaso-vagal sequel precipitated by a heavy operating session, by the intake of amphetamine, but despite the effectiveness of this reply we continue to receive suggestions embracing varied psychosomatic conditions under this generic term and which certainly simplifies the treatment thereof.

I now note the inclusion of nocturnal myoclonus (*Journal*, November 21, p. 1148), which I would have considered in varied effect to be common to all, increased by fatigue, and much more manifest in the lower species. Our little puppy is a past exponent of the art; he includes a manifest tremor of the masseter muscles with same and would not dream of going to sleep without such accompanying enjoyment. Like the knee-jerk, it would be the absence of them that would portray the abnormality, not their presence, and unless we regain our sense of perspective we shall soon be including all forms of sleep-association states, dreams, somnolence, somnambulism, and narcolepsy as epileptic aberration.—I am, etc.,

Tipton, Staffs. L. H. EUNSON.

SIR,—Arising from your annotation on this subject (*Journal*, November 21, p. 1148), I would like to draw attention to the involuntary jerking which occurs in some people when taking antihistamine drugs. This usually occurs at night and is commoner in the legs. The symptom was first noticed with promethazine hydrochloride, but has since occurred with chlorcyclizine hydrochloride, diphenhydramine hydrochloride, and mepyramine maleate. My experience with the other antihistamines has been limited, and it is quite possible that the jerking may occur with any one of this series of drugs. The exact incidence of this symptom is difficult to estimate. It may not be spontaneously complained of, but if specific inquiries are made it is found to be quite common. In some cases the jerking may be associated with restlessness and general excitement.

That nocturnal myoclonus may be linked with epilepsy is also interesting in connexion with the antihistamines, as it is known that these drugs may precipitate fits in known or potential epileptics. They have also been shown to increase the E.E.G. abnormally in epileptics.[1] In my own experience fits have been precipitated on four occasions by antihistamines and a history of fits is, in my opinion, a clear contra-indication to antihistamine therapy.—I am, etc.,

Bristol. ROBERT P. WARIN.

REFERENCE

1 Churchill, J. A., and Gammon, G. D. (1949). *J. Amer. med. Ass.*, **141**, 18.

POINTS FROM LETTERS

The General Practitioner and the Psychiatrist

Dr. JOAN W. KIPLING (Hull) writes: I should like to endorse Dr. G. L. Russell's doubt (*Journal*, October 24, p. 939) that "the majority of marital problems can be dealt with satisfactorily by the general practitioner." While some marriages are marred by comparatively simple and well-defined factors—for example, sex difficulties, sterility, lack of economic co-operation—many more are affected by a combination of several factors. If the G.P. lacks wisdom, interest, and, above all, time to deal with marital disharmony he can in most areas call on the help of the Marriage Guidance Council, whose workers are trained to consider social, ethical, and legal, as well as medical and psychological, aspects of marriage and to refer to consultants in each of these fields any case of exceptional difficulty. Many G.P.s welcome help given in such time-consuming work, although many would no doubt undertake more of it themselves if time allowed. Some undergo the training offered by the National Marriage Guidance Council.

Paroxysmal Paralytic Myoglobinuria

Dr. J. D. ROSANELLI (Tortola, British Virgin Islands) writes: In connexion with the discussion of the aetiology of this disease in the paper by Dr. Stephen D. Elek and Mr. Hugh F. Anderson (*Journal*, September 5, p. 533), it is noteworthy that myoglobinuria is invariably associated with creatinuria. Creatinuria regularly disappears on the administration of riboflavine (Hoff, F., 1948, *Medizinische Klinik*, Thieme, Stuttgart, and *Klinische Physiologie und Pathologie*, 1952, Thieme, Stuttgart). It is tempting to speculate that the experimental diet used by Ågren (*Svenska LäkT.*, 1944, **41**, 665) was not only deficient in aneurine but also in riboflavine. It is regrettable that the phenomenon of the "idiomuscular bulge" and the usually concomitant creatinuria have not been observed in this case.

Eponyms

Dr. W. E. MEDD (Farnham Common, Bucks) writes: There is a dark movement gaining ground which teaches that the names of diseases should be descriptive and not eponymous: thyrotoxicosis not Graves's disease; not Von Recklinghausen's disease but hyperparathyroidism. May I expound an apologia for the eponym? I like names that have a ring of history, names that recall those who were mighty physicians in palmier days. Surely a patient with Addison's disease can feel that he is merely making a small sacrifice for the perpetuation of the memory of the greatest of the Guy's triumvirate; whereas if he had adrenal hypocorticalism even that crumb of comfort would be denied him. How delightful to have Albright's syndrome; but if one contracted polyostotic fibrous dysplasia one would feel that one was falling to bits. The full glory of the eponym is reached in the multiple-barrelled form: Hand-Schüller-Christian, Rendu-Osler-Weber—those give the tongue something to roll round, and you can almost smell the mothballs in their morning coats and dear old top-hats. Let us condemn dull impersonal names, utility names in a utility age. Can we do no better than X disease or Q fever?

Cancer and the Psyche

Dr. E. JOYCE PARTRIDGE (Exeter) writes: I wish to put forward a plea that some of the money spent on research into the causes of cancer be directed into psychosomatic channels on the grounds that there may well be something in the attitude of mind (either conscious or unconscious) of the cancer victim which predetermines the development of the malignant cells. It has been suggested that it is changes in the body fluids which precede and invite the wanton multiplication of a given cell—i.e., initiate its cancerous growth. If this be so it is worth while to recall that the body fluids are those representatives of the soma which most readily respond to the activities of the psyche: tears, the dry mouth and the polyuria of fear, the changes in the gastric juice accompanying anxiety and mucous colitis, to mention but a few obvious examples.

Breast-feeding in Oxford

Dr. STELLA RING (Bexley) writes: Dr. Grace H. Walker (*Journal*, October 31, p. 995) is surely putting the cart before the horse. Breast-feeding is an expression of maternal love, not a cause, and as such is of incalculable value to the mother and the child. Artificial feeding can be an eminently satisfying experience, and some mothers even feel thirst and breast fullness when giving a bottle; but many more have to be comforted because they themselves are frustrated, however well the baby grows, by the failure of such a link.

Obituary

BASIL HUGHES, D.S.O., M.B., F.R.C.S.

Mr. Basil Hughes, for many years honorary surgeon to the Bradford Royal Infirmary, died in the Hospital of St. John and St. Elizabeth in London on November 21 at the age of 75.

Basil Hughes was the son of Captain J. E. Hughes, R.N., and was born in the village of Hales, Staffordshire, on March 30, 1878. He was educated at Eastman's Royal Naval Academy and at Selwyn College, Cambridge, where he took the mathematical tripos in 1900. He was some time making up his mind about what career to take up, hesitating between music, veterinary science, and school teaching. In 1904 he graduated B.Sc. at London University. He then decided to study medicine, and he entered King's College Hospital Medical School with a Sambrooke scholarship. His student career continued as brilliantly as it had begun, for he was awarded the second-year medical student scholarship and the Jelf medal in 1906 and the Tanner prize and a senior scholarship two years later. He qualified in 1909, graduated M.B. at Cambridge in the following year, and took the F.R.C.S. in 1911. After holding the appointments of house-physician and house-surgeon at King's College Hospital, he became casualty officer at the Royal Free Hospital, house-surgeon at Paddington Green Children's Hospital, and clinical assistant at The Hospital for Sick Children, Great Ormond Street. He then moved to Yorkshire to become pathologist and resident surgical officer at the Bradford Royal Infirmary, an appointment he held from 1911 to 1913.

On the outbreak of war in 1914 Hughes left his newly established practice as a consulting surgeon to enter the R.A.M.C. as a lieutenant, becoming regimental medical officer, first, of the 6th battalion and then of the 5th battalion of the West Yorkshire Regiment. Later he served as a surgical specialist and finally as officer in charge of the surgical division of general hospitals in France and Salonika, attaining the rank of major. It was when he was in Salonika that he was called upon to operate on the Serbian Minister of War, who had a depressed fracture of the skull. Hughes was twice mentioned in dispatches, and in 1918 he was awarded the D.S.O. and the Serbian Order of St. Sava for his services. He made a great reputation as a military surgeon, for he was a rapid and gentle operator. Quick to point out the danger of underrating shock, he also took exceptional pains to maintain asepsis during the treatment and dressing of wounds.

After the war Hughes returned to Bradford, and in 1919 he was appointed honorary surgeon to the Children's Hospital and a surgical specialist under the Ministry of Pensions. Three years later, after his appointment as senior surgeon to the Bradford Municipal General Hospital, he was elected to the staff of the Bradford Royal Infirmary as assistant honorary surgeon. Later he became honorary consulting surgeon to both institutions. In the last war Hughes's experience in the treatment of wounds was invaluable, and from the time of the Dunkirk evacuation until the end of the war he operated on a large number of wounded men, many of whom were admitted to St. Luke's Hospital. In 1943 he was elected a founder fellow of the International College of Surgeons in recognition of his standing as a surgeon and of his contribution on the classification of war wounds in the book *Surgery of Modern Warfare* (1941), edited by Mr. Hamilton Bailey. He was also a founder fellow of the Association of Surgeons of Great Britain and Ireland. His experiences in the war of 1914–18 provided him with the material for *War Surgery, from Firing Line to Base*, a book written in collaboration with Dr. H. Stanley Banks, who contributed the chapters on the bacteriological aspect of war surgery. Hughes was also a frequent contributor to the medical journals during the height of his career.

Relinquishing his hospital appointments in 1945, he retired to Cornwall, where, until he had a serious illness a year ago, he greatly enjoyed the management of his 56-acre farm at Par. He married Miss Norah Blayney, formerly well known as an actress, in 1932, and she survives him.

We are indebted to Mr. H. HAMILTON STEWART for the following appreciation: I had the good fortune, in my early days, to be assistant surgeon at the Bradford Royal Infirmary under Mr. Basil Hughes, and I shall always consider it a great privilege to have worked with him. He possessed a most colourful personality, due in part, no doubt, to his Welsh ancestry. He was a musician and a mathematician, and agriculture also interested him. After retiring from a very active life as a surgeon he took an agricultural course at Cambridge before he settled down to run his own farm in Cornwall. It must be rare for such diverse qualities to be present in any one man.

Hughes was cheerful and good-tempered, and he could often be heard coming along the corridors whistling a tune. He had at one time a great phase for "keeping himself alkaline," as he believed that this was necessary for good health. His lunch on a long operating day would consist of a plate of raw vegetables, which he would eat with apparent relish. He was very fond of driving in an open car even in the depths of winter, when most men after operating would have feared pneumonia. As a surgeon, he was indefatigable, and he was always alive to any advances. He did a great deal to enhance the prestige of Bradford as a surgical centre. Patients came from all parts of the country to be treated by him.

He was a most dexterous surgeon, with fine hands, and there were few in this country who were his equal in surgical technique. As a result of his experience as a children's surgeon he was an advocate of small incisions. I should say that one of the main reasons for his great success as a surgeon was his gentleness in handling human tissues. He will long be remembered by his friends and by his numerous patients.

Sir LANCELOT BARRINGTON-WARD

K.C.V.O., Ch.M., F.R.C.S., F.R.C.S.Ed.

A. J. M. B. writes: Sir Lancelot Barrington-Ward (whose obituary notice was published in last week's *Journal*) was senior surgeon of the Wood Green and Southgate Hospital for 18 years, and had been on the surgical staff for over 20 years before that. Those of us general practitioners who knew him there will always remember with affection his Wednesday visits. Exactly at 2.30 p.m. he would walk in briskly, his trim athletic figure reminding us of the days when he was a Rugby international and a redoubtable amateur boxer at Edinburgh University. Glancing at us with an expression that seemed to be an amusing blend of courtesy and raillery he would bow deeply and ask; "What problems have you for me to-day?" He set himself a high standard of work and expected it from others. As a member of the staff once said, "When the chief arrives, this hospital springs to attention." It was certain that he commanded deep respect as well as affection. The hospital, though very small compared with the others which he attended, was in a sense one of his hobbies. He had watched its growth and develop-

ment with loving care, had acted as chairman of the hospital council for 13 years, and was ever ready to devote time to promoting the welfare of the patients and staff. Countless numbers of our patients in the district have good cause to be grateful for his wise advice and surgical skill; and we, his colleagues, mourn him as a friend and cherish his memory.

Dr. WILLIAM KERR RUSSELL, who died on November 5 after a prolonged period of ill-health, was born at Stewarton, Ayrshire, on April 12, 1874. Educated at Kilmarnock Academy and Glasgow High School, he graduated M.B., C.M. at Glasgow University in 1897. He settled in practice at Sunderland in 1899 and retired in 1948 on account of ill-health. He was a very active member of the B.M.A. and an ex-chairman of the Sunderland Division. He was also a founder member of the West End Medical Society and ex-chairman and member of the council of the Glasgow and Aberdeen North-eastern University Club. "Willie," as he was affectionately known to his colleagues, was a first-class example of the good family doctor of a previous generation. He was guide, philosopher, and friend to his patients and nothing was allowed to come between him and their welfare. A memorial service was held at Trinity and St. James's Presbyterian Church, where he had been an elder for 43 years.—J. S. M.

Medical Notes in Parliament

CLEAN FOOD BILL

The Food and Drugs (Amendment) Bill was given a second reading in the House of Lords on November 24.

Viscount WOOLTON, who moved it, said that its first main purpose was to ensure a higher standard of cleanliness in places where food was prepared or handled. Under Clause 6 the Ministers of Food and Health were given powers to make *ad hoc* regulations suited to the conditions of many different kinds of businesses and foods. A start would be made with new hygiene regulations, and after that would come registration of all premises where food was stored or handled, beginning with premises where food infection was most likely to occur, such as catering establishments. The second main purpose was to bring up to date the protection of the public against the use of substances and processes liable to render food injurious to health. It was sought to do this by preventing the addition of any substance to food, or the abstraction of any constituent, or the use of any treatment in preparing food, which made it injurious to health. The present law had proved inadequate, particularly in dealing with what was described as chronic toxicity. This was dealt with in Clause 5, which laid it down that the cumulative effect of additions or abstractions, or ingredients or processes, must be taken into account when the possibility of injury to health was being thought of.

The machinery by which the Bill's provisions would be put into effect would be, broadly speaking, by administrative control of standards of food hygiene and composition from the centre, by way of regulations, and it would then be for local authorities to execute and enforce these regulations. It was intended in due course to introduce a consolidating measure. Answering a point made by Lord Silkin, he stated that it was certainly intended that the Bill should cover restaurants.

Cleanliness in Restaurants

Lord WEBB-JOHNSON said it was fitting that a member of the medical profession should welcome the Bill, and it was gratifying that definite action was being proposed. The parts of the Bill that appealed to him were those that dealt with misleading advertisements and labels, those which imposed requirements, and those that were to regulate the addition of chemicals. He welcomed the assurance that the Bill was to apply to restaurants. Clause 6 referred to the provision, maintenance, and cleanliness of sanitary and washing facilities, apparatus, furnishings, and utensils, but there was no reference to the personnel. It was extremely difficult to ensure that the workers would be clean, not only in themselves but in their clothing and so on, but it was a matter of first importance, and had been so treated in the Factory Acts. It had been suggested that the public could be a big controlling factor in imposing the adoption of cleanly methods in the serving of food. That was true, but the public were not particularly well informed on the statutory requirements, nor necessarily well educated in the correct way of handling food.

Lord HADEN-GUEST said that the Bill, with some amendments, would be a valuable safeguard of the national health. Not everything could be done directly by the drafting of the Bill, and it would be necessary to have more regulations, not fewer, to carry out its purpose, and they should be written in plain English so that they could be clearly understood. There was one point which he was not sure could be dealt with by regulations, although they could be made. In food shops and all places concerned with the distribution of food it was necessary to have a higher standard of personal cleanliness, and he believed that could come only from health education and training.

Lord SALTOUN gave some figures showing the extent of the habit of eating out, and the number of cases of food-poisoning. He quoted the Caterers' Association as stating that they sold some 10,000 million meals a year to the public, and the Ministry of Health Chief Medical Officer's analysis of the 255 outbreaks of food-poisoning that were traceable in the 21 months from April 1, 1950, to December 31, 1951—41 of them occurred in hotels, restaurants, and cafés, and 31 in works canteens. More recent figures for the first nine and a half months of this year showed that, out of 700 traceable outbreaks, 27 occurred in hotels, etc., and 17 in works canteens. Lord SEMPILL repeated Sir Edward Mellanby's criticisms about food manipulation and the use of agene in flour, and Viscount BLEDISLOE protested about the amount of advertising "booming" various foods and synthetic preparations as likely to enhance health or improve the general wellbeing.

Old-age Pensioners

Mr. R. H. TURTON, Parliamentary Secretary to the Ministry of Pensions and National Insurance, replying to a short debate on November 23 about the hardships of old-age pensioners, quoted the results of the national food surveys, which were instituted in 1951 and dealt with the calorie intake of the pensioners. Although the figures did not show a very bright picture, he said, they showed a considerable improvement. In January and February, 1951, the calorie intake was 7% below the requirements based on the B.M.A. scales. When the increase in retirement pensions was introduced last year the level rose to just over 100% of the B.M.A. requirements, and the most recent figures showed that for the first quarter of 1953 it was 4% over those requirements.

Fluoride Treatment of Teeth

Mr. WILLIAM ROSS on November 24 asked the Secretary of State for Scotland if he would state the areas in which an effort was being made to reduce dental decay by the application of solutions of sodium fluoride, and what knowledge had been gained from these efforts. Mr. J. STUART informed him that work of this kind had been carried out among schoolchildren in Dundee, Edinburgh, and Fife. While it promised to afford a measure of protection against dental decay, it would be some years before final conclusions could be drawn about its place in preventive dentistry.

Scottish Lunacy Laws

Mr. A. WOODBURN asked the Secretary of State for Scotland on November 26 whether he would make a further statement on the intentions of the Government to set up a

Royal Commission to consider and report on mental illness and deficiency in Scotland. Mr. J. STUART replied that the whole field was covered by the Committee on the Scottish Lunacy and Mental Deficiency Laws under the chairmanship of Lord Russell that reported in 1946. A further inquiry at this date was unnecessary, but he was considering the report and proposed in due course to lay a White Paper before Parliament as a basis for further discussion.

Fog Masks for Old People

Mr. B. TANNER asked the Minister of Health on November 26 whether, in view of the fact that most of the patients who would require masks as a protection from fog would be old people in the low income group, he would allow such masks to be issued free of any prescription charge. Miss PAT HORNSBY-SMITH, the Parliamentary Secretary, said that there were no grounds which would justify drawing a distinction between masks and other necessary drugs and appliances prescribed by general practitioners. Where the charge could not be met without hardship the usual simple arrangements for securing a refund applied.

Tuberculosis Waiting-lists

Mr. IAIN MACLEOD, Minister of Health, stated in reply to Brigadier F. MEDLICOTT on November 26 that the numbers of patients suffering from tuberculosis who were on the waiting-lists for admission to hospitals were 9,378 at the end of 1950, 7,096 in 1951, and 6,126 in 1952.

Vaccination Among Immigrants

Mr. S. P. VIANT asked the Minister of Health on November 27 whether entrants into Great Britain were asked to produce a certificate of vaccination against smallpox. Mr. IAIN MACLEOD said they were not normally, but if it was necessary to consider placing passengers from an infected area or craft under surveillance they might be asked whether they could produce evidence of recent vaccination.

Medico-Legal

ALLEGED FATAL BLOOD TRANSFUSION

Judgment was entered for the Southend Group Hospital Management Committee in the Queen's Bench Division on November 27 in an action in which it was alleged that the negligent administration of a blood transfusion at Southend General Hospital caused the death of a patient. On the third day of the trial, after hearing all the evidence, Mr. Justice Hilbery ruled that there was no case for the jury to consider.

The plaintiffs in the action were Mr. and Mrs. E. F. Webb, of Hadleigh, Essex. They claimed damages from the Management Committee in respect of the death at the hospital on November 21, 1951, of their son, Raymond L. Webb, aged 26. They alleged negligence by the house-surgeon, Dr. Joseph A. Ryan. It was stated that Dr. Ryan was not a defendant in the action, because he could not be traced. He was said to have returned to Canada, where he qualified. The Management Committee denied negligence, and pleaded further that Dr. Ryan was not their servant, although he was under contract to them at the time.

The plaintiffs contended that Dr. Ryan's only medical qualification was a degree obtained at Dalhousie, Nova Scotia, in May, 1951, and that he was not temporarily registered at the material time by the General Medical Council, and that he was not entitled to practise when he was appointed to his post at Southend General Hospital on August 18.

Raymond Webb entered hospital on October 28, 1951, and was successfully operated on for haemorrhoids on October 29. Between November 8 and 12 he had haemorrhages and was given blood transfusions. On November 18 the fourth blood transfusion was given, but was unsuccessful. Rigor set in, accompanied by nausea and high temperature, and the transfusion was discontinued. On November 21, after the patient's reluctance had been overcome, he was given another transfusion. He reacted in the same way as on the 18th. By 5 p.m. his temperature rose to over 103° F. (39.4° C.) and his pulse became imperceptible. In spite of treatment he died at 8 p.m. A post-mortem examination showed death to have been caused by toxaemia, due to infected blood, and it was plaintiffs' case that the infection was introduced into their son's system during the transfusion.

Mr. F. R. Overend, assistant secretary of the General Medical Council, said in evidence that at the time Dr. Ryan was not registered, but agreed that temporary registration would have been granted if Dr. Ryan had asked for it. The fact that Dr. Ryan was not registered had nothing to do with his qualifications or ability.

Dr. J. W. Lacey, pathologist at St. John's Hospital, Chelmsford, giving evidence of a post-mortem examination of Raymond Webb, said that death was due to the presence in the blood stream of *Bacterium coli-aerogenes*. There was no question of the blood groups being incompatible. Given the circumstances of the patient's death, everything unquestionably pointed to the fact that the blood given in the transfusion of November 21 contained an enormous number of these organisms. He agreed that fatal reactions could be caused by the presence in the transfused blood of dead bacilli, which would be extremely difficult to detect. That could happen without negligence on anybody's part.

An Unhappy Chance

The case for the Management Committee was that the death of Raymond Webb was an unhappy chance—one of those rare cases where fatal reactions followed the transfusion of blood which was both sterile and compatible.

Mr. J. J. Shipman, who was senior surgical registrar at Southend General Hospital in 1951, said Dr. Ryan was a competent young surgeon and his ability in administering a blood transfusion was above the average. The witness said he ordered the transfusion on November 21, and he considered it a reasonable decision. The patient's haemoglobin content was only 44%.

Dr. W. D. Nicoll, senior registrar in the department of pathology at the hospital, said that the blood used on November 18 and on November 21 was compatible and sterile. The blood used on November 21 was checked again on November 22. It was compatible, but a culture taken from it developed a heavy growth of *Bacterium coli*. This he thought was due to the fact that the bottle had been left uncapped in the ward for several hours.

Dr. D. C. Caldwell, consultant pathologist at the hospital, said he was not surprised that Dr. Lacey had found infection in an examination carried out five days after death. He thought it likely that the infection stemmed from the site of the operation. Cross-examined, he agreed that something in the transfused blood caused the patient's death, but he did not agree that there was infection in the blood. He did not know what caused death.

Dr. G. Discombe, pathologist at the Central Middlesex Hospital, gave evidence that he agreed with the conclusions arrived at by Dr. Caldwell.

At the conclusion of evidence Mr. Justice Hilbery said there was "not a shadow of evidence" to support the allegations of negligence against the hospital. One allegation which he said should never have been made was that concerning Dr. Ryan's non-registration. Dr. Ryan was a young man with full and proper qualifications obtained in Canada. An allegation that the hospital was negligent in entrusting the blood transfusion to a young man recently qualified was absurd, particularly as he was said in evidence to have been exceptionally competent. People were not entitled to make charges of negligence and put them on the record of the court, without some evidence to support them, in the hope that they might be able to discover something to justify them. There was no evidence that the bottle in question had become infected because of the way it had been handled by Dr. Ryan or anyone else.

Saying there was no evidence on which the jury could find a verdict for the plaintiffs, he entered judgment for the defendants.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending November 14 (No. 45) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	26	1	5	1	1	27	1	14	0	1
Dysentery	370	47	243	1	2	213	24	109	1	2
Encephalitis, acute	0	0	0	0		6	0	0	1	
Enteric fever:										
Typhoid	1	0	0	1		4	0	1	15	
Paratyphoid	1	0	1	0		2	0	1 (B)	0	
Food-poisoning	164	18		0		110	7		0	
Infective enteritis or diarrhoea under 2 years				21	31				10	23
Measles*	816	24	37	14	80	11,264	989	155	21	139
Meningococcal infection	30	5	14	1	1	30	3	17	0	
Ophthalmia neonatorum	32	2	5	1	1	34	4	10	0	
Pneumonia†	534	41	171	5		502	33	282	8	
Poliomyelitis, acute:										
Paralytic	66	1	27	4	7	81	6	5	2	3
Non-paralytic	29	4				36	3			
Puerperal fever§	246	27	12	1	1	211	23	12	0	2
Scarlet fever	1,400	96	217	37	51	1,976	166	381	22	115
Tuberculosis:										
Respiratory			146	20				124	19	
Non-respiratory			19	6				19	6	
Whooping-cough	2,410	126	285	53	60	1,449	80	74	28	108

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	2	0		0	0
Dysentery	0	0	1	0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	10	0	1	1	2	7	1	1	0	2
Influenza	10	0	2	1	1	10	0		0	
Measles		0	0	0	0		0		0	0
Meningococcal infection		0	1				0	2		
Pneumonia	209	27	20	6	4	176	35		5	5
Poliomyelitis, acute	6	0			0	2	0			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis:										
Respiratory	96	10	8	3	1	117	10	9	1	3
Non-respiratory		2	1	2	2		3	2	0	3
Whooping-cough	4	0	0	0	0	1	1	1	0	0
Deaths 0–1 year	191	26	30	11	19	181	31	25	11	14
Deaths (excluding stillbirths)	5,269	695	575	133	169	4,803	693	469	100	164
LIVE BIRTHS	6,752	982	853	205	361	6,930	1058	760	207	402
STILLBIRTHS	205	18	25			185	13	23		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

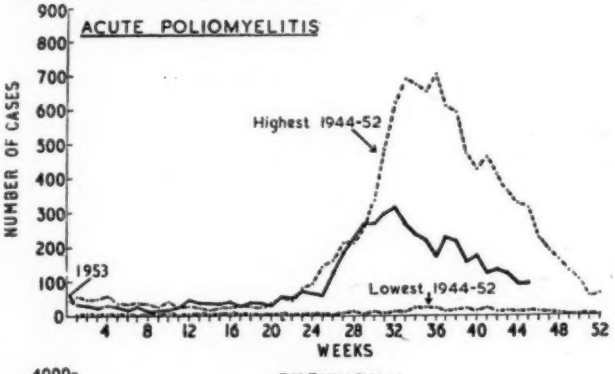
Industrial Accidents and Diseases

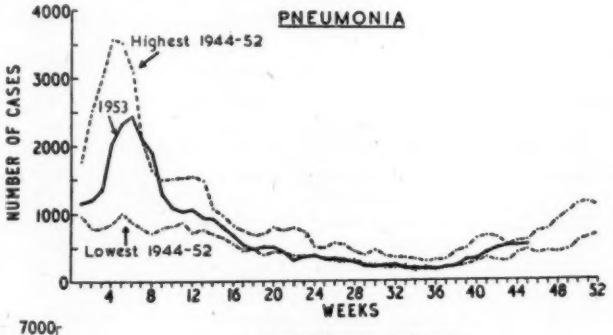
The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in October was 124, compared with 117 in the previous month and 116 (revised figure) in October, 1952.

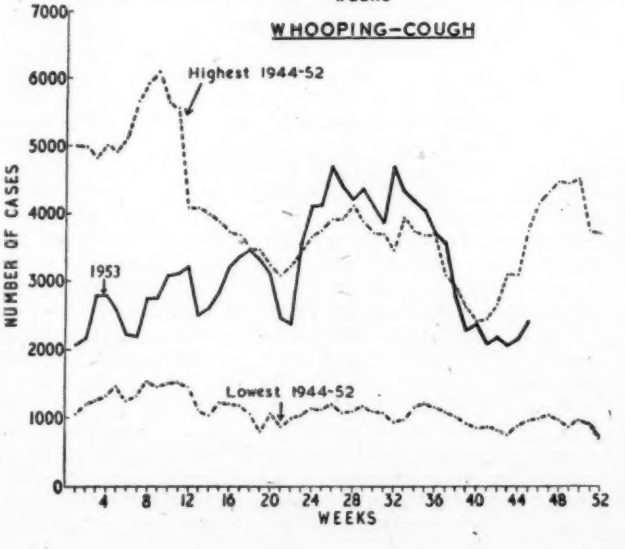
The number of cases of industrial diseases in the United Kingdom reported during October was as follows: lead poisoning, 1; other poisoning, 13; anthrax, 3; epitheliomatous ulceration, 8; chrome ulceration, 13; total, 38. There were no deaths.—*Ministry of Labour Gazette*, November, 1953.

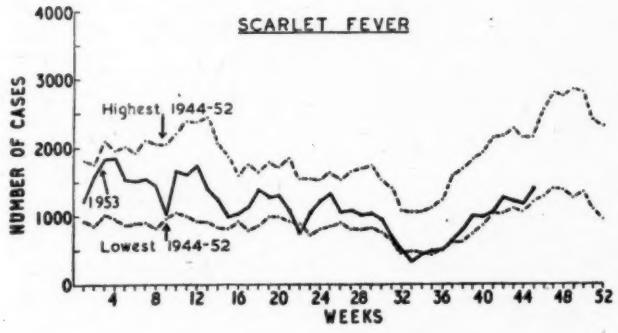
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The largest variations in the notifications of infectious diseases in England and Wales during the week ending November 14 were increases of 235 for whooping-cough, from 2,175 to 2,410, and 213 for scarlet fever, from 1,187 to 1,400, and a decrease of 214 for measles, from 1,030 to 816.

The largest rises in the incidence of scarlet fever were 46 in Lancashire, from 165 to 211, and 38 in London, from 58 to 96. The largest fluctuations in the local returns of whooping-cough were rises of 76 in Yorkshire West Riding, from 195 to 271, 55 in Kent, from 43 to 98, and 55 in Norfolk, from 43 to 98, and falls of 49 in Staffordshire, from 125 to 76, and 33 in Surrey, from 91 to 58. The largest decreases in the number of notifications of measles were 79 in Cumberland, from 128 to 49, and 79 in Lancashire, from 248 to 169, while the largest increase was 34 in Staffordshire, from 88 to 122. 26 cases of diphtheria were notified during the week, being 8 more than in the previous week. The chief feature of the returns was a rise in Staffordshire from 5 to 13. 7 of the 13 cases were notified in Coseley U.D., where 7 cases were notified a fortnight earlier.

95 cases of acute poliomyelitis were notified. These were 6 more for paralytic and 5 fewer for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 12, Lancashire 11, Dorsetshire 7 (Wimborne and Cranborne R.D. 5), London 5, and Lincolnshire 5.

Notifications of dysentery numbered 370, and were 12 more than in the preceding week. The chief centres of infection were Yorkshire West Riding 98 (Bradford C.B. 60, Halifax C.B. 17), Yorkshire North Riding 18 (Middlesbrough C.B. 18), Lancashire 54 (Manchester C.B. 11, Bolton C.B. 9), London 47 (Islington 8), Middlesex 25 (Willesden M.B. 9), Warwickshire 17 (Birmingham C.B. 17), and Leicestershire 11 (Leicester C.B. 11).

In Scotland 105 cases of dysentery were notified in Glasgow and 37 in Edinburgh.

Week Ending November 21

The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,613, whooping-cough 2,510, diphtheria 28, measles 793, dysentery 362, acute poliomyelitis 88, paratyphoid fever 9, and typhoid fever 2.

The Services

Surgeon Commander Robert M. Coplans, R.A.N., Officer in Charge of the Royal Australian Naval School of Air Medicine and Naval Specialist in Hygiene, has been appointed Honorary Physician to the Governor-General of Australia.

Colonel P. R. Hawe, T.D., R.A.M.C., T.A., has been appointed Honorary Colonel of a Territorial Army Unit, in succession to Colonel J. P. Clarke, T.D., R.A.M.C., T.A., whose tenure has expired.

Medical News

Royal Society.—Last Monday Dr. E. D. Adrian, O.M., delivered his presidential address to the Royal Society. The great volume of scientific publication nowadays made it difficult for him, he said, to pick out any one discovery for particular mention. "There has been great activity in many lines, but for the time being we seem to have passed the stage of really startling discoveries." In the most promising fields the general line of advance could be foreseen for a few years at least. It would be safe to expect, for instance, valuable developments in the fields of synthetic chemistry and in our understanding of the structure of proteins, the nature of viruses, and the action of enzymes. "But we are well prepared for them: they will not startle us unless they show some fault in the accepted theories." Dr. Adrian then spoke of some of the difficulties created by the rapid expansion of science. On the one hand, boundaries between different scientific disciplines were becoming blurred; on the other, new specialist groups were arising. Long ago it had passed the competence of one mind to keep the enormous territory of science in focus. At the close of his address Dr. Adrian alluded to the physical basis of memory. "We must start each morning with our brain structure modified by what happened to it the day before," he said. It was now possible to examine the reactions of a single nerve cell by thrusting a microelectrode into it, and the changes produced by repeated activity were being studied. However, the storage process might well involve a chemical as well as a physical reorganization. Evidence was accumulating that the transmission of signals from one cell to another depended on the release from the cell terminals of stimulating molecules and their rapid destruction by enzymes.

Scientific Exhibition.—At the B.M.A. Annual Meeting next year in Glasgow there will again be a scientific exhibition, open from July 5 to 9. This event proved very popular at the meetings at Dublin and Cardiff. To the exhibitor it offers unique opportunities of discussing his work with colleagues from at home and abroad. Medical research and current medical practice and techniques are suitable subjects for exhibition. Space is limited, so potential exhibitors are advised to apply for stands as soon as possible, and certainly not later than December 31. Full information and application forms can be obtained from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

Air Attendants.—The St. John Ambulance Brigade can provide air attendants for patients travelling by air both in Britain and abroad. The attendants are qualified in air duties and emergency midwifery in addition to first aid and nursing. The service is voluntary, and the only payment is the attendant's fare and reasonable out-of-pocket expenses. All attendants are fully insured. At present this service is limited to British European Airways, but it is hoped to extend it soon to other air corporations. Applications for attendants should be made to the Officer in charge of Register, St. John Ambulance Brigade Headquarters, 8, Grosvenor Crescent, London, S.W.1 (telephone, Sloane 9861). If special equipment is likely to be required the doctor should give warning of this beforehand.

Anglo-French Exchange Bursaries.—Applications are now invited for the bursaries which will be awarded in 1954 to young British doctors under the exchange scheme arranged by the French Embassy in London between the Institut National d'Hygiène in Paris and the Ciba Foundation in London. The value of the French grants is 60,000 francs a month, tax free, and they will be awarded for periods of two to four months to doctors who wish to obtain clinical experience or carry out medical research in France. Since the aim of the exchange is to spread in each country knowledge of achievements, outlook, and methods on the other side of the Channel, preference will normally go to candi-

dates who are in teaching, or in posts where they can pass on the experience they have acquired. Application forms may be obtained from Dr. G. E. W. Wolstenholme, Ciba Foundation, 41, Portland Place, London, W.1. The closing date for applications is February 22, 1954.

Medical Artists.—The Medical Artists Association of Great Britain will shortly hold an examination of work submitted by those seeking membership. The last date for entries is January 30, 1954. Entry forms may be obtained from the honorary secretary, the Rotunda, the Radcliffe Infirmary, Oxford.

First-aid Resuscitation.—On the advice of the Medical Research Council, the mixture of oxygen and carbon dioxide formerly carried in local authority ambulances for first-aid resuscitation is now being replaced by pure oxygen.

Professor B. W. Windeyer has been appointed Dean of the Middlesex Hospital Medical School. Professor Windeyer graduated in Sydney, Australia, in 1927. Since 1942 he has occupied the London University Chair of Radiology (Therapeutic) at the Middlesex Hospital. He succeeds Sir Harold Boldero.

Miss Grace Hoare, personal assistant to the Editor of the *British Medical Journal,* has retired after 45 years' devoted service to three of the *Journal's* editors.

COMING EVENTS

The 10th International Congress of Medicine in Sport will take place in Belgrade from May 19 to 22, 1954. Further information may be obtained from Dr. Vojin Smodlaka, Belgrade, Deligradska 27, Yugoslavia.

International Society of Orthopaedic Surgery and Traumatology.—The sixth congress of the International Society of Orthopaedic Surgery and Traumatology will be held in Berne, Switzerland, from August 30 to September 3, 1954. All correspondence should be addressed to the secretary-general of the Society, Mr. J. Delchef, M.D., 34, rue Montoyer, Brussels, Belgium.

NEW ISSUES

British Journal of Ophthalmology.—The next issue (Vol. 37, No. 12) will be available in a week's time. The contents include:

OCULAR COMPLICATIONS OF DIABETES MELLITUS. G. I. Scott.
OCULAR COMPLICATIONS OF DIABETES MELLITUS. Leonard H. Howells.
LENS EXTRACTION IN DIABETIC PATIENTS. A. B. Nutt.
OCULAR MANIFESTATIONS IN LÖFFLER'S SYNDROME. D. M. J. Velzeboer.
AMYL NITRITE TEST IN PRIMARY GLAUCOMA. G. Cristini and N. Pagliarani.
SMALL VOLUNTARY MOVEMENTS OF THE EYE. B. L. Ginsborg.
SYMPATHETIC OPHTHALMIA FOLLOWING AN OPERATION FOR RETINAL DETACHMENT. Walter Kornblueth and Richard Stein.
UNUSUAL CASE OF DOUBLE PRIMARY TUMOUR. Ida Mann, P. C. Yates, and J. P. Ainslie.
THE LEGEND AND SHRINE OF SAINT TRIDUANA. John Foster.

Issued monthly; annual subscription £4 4s., single copy 8s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, December 7

●HUNTERIAN SOCIETY.—At Talbot Restaurant, London Wall, E.C., 7 for 7.30 p.m., dinner meeting. Discussion: A Pain in the Neck, to be opened by Dr. J. W. Aldren Turner and Mr. H. Osmond-Clarke.
●POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Professor A. Haddow: Recent Trends in the Experimental Pathology of Cancer.
ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: The "Refraction Case." Six Factors Producing Good Sight.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., First Harben Lecture by Sir Henry Dale, O.M., F.R.S.: Changes and Prospects in Medicinal Treatment (illustrated).
UNIVERSITY COLLEGE, LONDON: DEPARTMENT OF BIOCHEMISTRY.—At Physiology Theatre, 4.45 p.m., public lecture by Dr. H. Gutfreund: Molecular Forces in Protein Solutions—(1) Molecular Interaction in Protein Solutions.

Tuesday, December 8

CHELSEA CLINICAL SOCIETY.—At South Kensington Hotel, 7.30 p.m., dinner, followed by a discussion: Dictators and Their Doctors, to be opened by Mr. A. Dickson Wright.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. D. Samman: Reticulosis.
LONDON UNIVERSITY.—At Anatomy Lecture Theatre, University College, 5.30 p.m., Special University Lecture in Psychology by Professor Otto Koehler (Freiburg): Thinking Without Words. Illustrated with lantern slides and films.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., FitzPatrick Lecture by Dr. Maurice Davidson: Medicine in Oxford, A Historical Romance: From the Laudian Code (A.D. 1636) to the Early XIXth Century.
ROYAL EYE HOSPITAL.—5 p.m., Professor Arnold Sorsby: Nature of Congenital Anomalies.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Second Harben Lecture by Sir Henry Dale, O.M., F.R.S.: Changes and Prospects in Medicinal Treatment (illustrated).
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., Mr. Aleck W. Bourne: Non-malignant Conditions of the Cervix.
WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Mr. I. R. McCaul: Investigation of Cerebral Tumour.

Wednesday, December 9

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Reticulosis.
INSTITUTE OF NEUROLOGY.—5 p.m., Dr. H. Hécaen (Paris): The Balint's Syndrome and its Minor Forms.
INSTITUTE OF PSYCHIATRY.—At Maudsley Hospital, 5.30 p.m., public lecture by Dr. Eliot Slater: The M'Naghten Rules and Modern Concepts of Responsibility.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. J. G. Sandrey: Urological Emergencies in General Practice.
LIVERPOOL MEDICAL INSTITUTION.—At Liverpool Royal Infirmary, 3 p.m., clinical meeting.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Professor G. MacG. Bull: Tests of Renal Function.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., Bradshaw Lecture by Sir Reginald Watson-Jones: Fracture Treatment in the Next Half Century.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—5 p.m., Third Harben Lecture by Sir Henry Dale, O.M., F.R.S.: Changes and Prospects in Medicinal Treatment (illustrated).
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Theatre, 5 p.m., lecture-demonstration by Dr. J. D. W. Pearce: Psychological Medicine.
SOCIETY OF CHEMICAL INDUSTRY: FOOD GROUP: NUTRITION PANEL.—At Medical Society of London, 6.30 p.m., Dr. R. Passmore: Some Recent Investigations of Human Calorie Requirements.

Thursday, December 10

ALFRED ADLER MEDICAL SOCIETY.—At 11, Chandos Street, London, W., 8 p.m., Dr. L. P. E. Laurent: Psychosomatic Effects of Obesity.
●INSTITUTE OF CARDIOLOGY, National Heart Hospital.—9.30 a.m., Dr. Maurice Sokolow (California): Quinidine.
●INSTITUTE OF CHILD HEALTH AND INSTITUTE OF NEUROLOGY.—At National Hospital, Queen Square, W.C., 5.30 p.m., Dr. B. H. Kirman: Epilepsy and Paralytic Syndromes.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Superficial Fungus Infections of the Skin.
PHARMACEUTICAL SOCIETY OF GREAT BRITAIN.—7.30 p.m., Professor A. A. Miles: Biological Standards.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—3.30 p.m., Professor G. MacG. Bull: Tests of Renal Function.
ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Dr. J. S. Wilson: Work of the Public Health Laboratory Service.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., FitzPatrick Lecture by Dr. Maurice Davidson: Medicine in Oxford, A Historical Romance: From the Early XIXth Century to A.D. 1914. Epilogue.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Robert Jones Lecture by Mr. St. J. D. Buxton: Arthroplasty.
ROYAL SOCIETY.—4.30 p.m., Sir Francis Walshe, F.R.S.: The Contribution of Clinical Observation to Cerebral Physiology.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—7.30 p.m., Dr. Henry Foy: Influence of the Intestinal Flora on the Synthesis of Haemopoietic Factors in the Megaloblastic Anaemia of Africans.
ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Dr. C. M. Fletcher: Observer Error in Clinical Medicine.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Sir Paul Mallinson: psychiatry demonstration.

Friday, December 11

INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. P. D. Samman: Reticulosis.
OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., Dr. Leonard Colebrook, F.R.S.: Emile Roux (December 17, 1853-1933).
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4.30 p.m., Professor G. MacG. Bull: Tests of Renal Function.
ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Symposium: Nephritis.
SOCIETY OF PUBLIC ANALYSTS: BIOLOGICAL METHODS GROUP.—At Anatomy Lecture Theatre, University College, 2.30 p.m., joint meeting with Pharmaceutical Society. Symposium on The Assay and Detection of Pyrogens. Papers by Mr. T. D. Whittet, B.Sc., Ph.C., Mr. K. L. Smith, M.P.S., and Mr. M. Dawson, Ph.C., and Professor J. P. Todd, Ph.D., Ph.C., F.R.I.C.

Saturday, December 12

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, London Hospital Medical College, 11 a.m., 324th meeting. Scientific papers.
SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At King's College Hospital Medical School, 10.30 for 11 a.m., annual meeting. Demonstration by Dr. Clifford Hoyle: Sarcoidosis—assisted by Dr. John Dawson and Dr. Gordon Mather.

APPOINTMENTS

ABSE, DAVID WILFRED, M.D., D.P.M., Full-time Associate Professor of Psychiatry, the School of Medicine, University of North Carolina, Chapel Hill, North Carolina, U.S.A.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—Pamela M. Hellings, M.B., Ch.B., D.A., Anaesthetic Registrar at United Norwich Hospitals; J. G. Weir, M.B., Ch.B., Registrar in Psychiatry, Addenbrooke's Hospital and Fulbourn Hospital.

EVANS, RICHARD GERWYN, M.B., B.Ch., C.P.H., Assistant Medical Officer of Health, Breconshire County Council.

HIRD, GORDON, M.B., Ch.B., D.P.H., Assistant County Medical Officer of Health, Warwickshire.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—H. E. Lockhart-Mummery, M.Chir., F.R.C.S., Part-time Senior Surgical Registrar; Doreen P. Pallot, M.B., B.S., D.A., Resident Anaesthetic Registrar; Josephine J. Candy, M.B., B.Ch., and Marion R. MacKay, M.B., B.Ch., Junior Resident Anaesthetists; N. J. Rothfield, M.B., B.S., D.C.H.,

House-physician; Joan M. Wagner, M.B., B.Ch., M.R.C.P., and Joyce B. Burke, M.D., M.R.C.P., D.Obst.R.C.O.G., D.C.H., Whole-time Assistant Medical Registrars.

LIVERPOOL REGIONAL HOSPITAL BOARD.—E. F. B. Cadman, M.D., M.R.C.P., D.C.H., Part-time Visiting Consultant Physician to Hospitals in Southport Area; A. G. McCarey, M.D., D.M.R.D., Dip.Rad., Consultant Radiologist to East Liverpool Area; J. H. E. Carmichael, M.D., D.M.R.D., Dip. Rad., Assistant Radiologist to East Liverpool Area.

LONDON TRANSPORT: DEPARTMENT OF THE CHIEF MEDICAL OFFICER.—J. L. Fyfe, M.B., Ch.B., D.I.H., Senior Medical Officer; D. M. Evans, M.B., B.Chir., Medical Officer in charge of North-east Division Medical Centre, Manor House; C. E. Sefton Myers, M.R.C.S., L.R.C.P., Medical Officer at North-east Division Medical Centre.

LYCETT, C. D. L., M.D., D.P.H., County Medical Officer of Health and Principal School Medical Officer, Wiltshire County Council.

MCGOVERN, JAMES, M.B., Ch.B., D.P.H., Assistant County Medical Officer for Shropshire and Medical Officer of Health for the Ellesmere Urban and Rural, Wem Urban and Rural, and Whitchurch Urban Districts.

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—M. Klein, M.D., D.O.M.S., Part-time Ophthalmic Surgeon (Consultant), London Jewish Hospital; J. H. Dixon, M.B., B.Chir., D.A., Part-time Anaesthetist (Consultant), Black Notley and Broomfield Hospitals; D. Zuck, M.B., Ch.B., D.A., F.F.A. R.C.S., Full-time Anaesthetist (Consultant), Chase Farm Hospital and Group; Helen M. Mayer, M.R.C.S., L.R.C.P., M.R.C.O.G., Part-time Gynaecologist (Consultant), Mildmay Mission Hospital; S. F. Hans, M.D., F.R.C.S., M.R.C.O.G., Part-time Obstetrician and Gynaecologist Consultant), Epping Group of Hospitals; B. Cohen, M.B., Ch.B., F.R.C.S., D.L.O., Part-time Ear, Nose, and Throat Surgeon (Consultant), North Middlesex Hospital; H. S. A. Henry, M.B., B.Ch., F.R.C.S.I., D.P.H., D.L.O., Part-time Ear, Nose, and Throat Surgeon (Consultant), Queen Mary's Hospital for the East End; H. J. M. Stratton, F.R.C.S.Ed., D.L.O., Part-time Ear, Nose, and Throat Surgeon (Consultant), Bethnal Green Hospital; D. C. Arnott, M.B., B.S., D.C.H., D.Phys.Med., Part-time Physician in Physical Medicine (Consultant), Harold Wood and Brentwood District.

O'NEILL, THOMAS, M.D., M.Ch., F.R.C.S., Surgeon, Sir Patrick Dun's Hospital, Dublin.

PLEWS, WILLIAM R., L.R.C.P.&S.Ed., L.R.F.P.&S.Glas., D.P.H., D.Obst.R.C.O.G., Depute Medical Officer of Health and Depute Port Medical Officer, Burgh of Greenock.

SCADDING, F. H., M.D., M.R.C.P., Assistant General Physician on Consultant Staff of Middlesex Hospital.

SIMPSON, RONALD G., M.D., M.R.C.P., Physician Consultant in Geriatrics for Perth and Perthshire District of Scotland, Eastern Regional Hospital Board (Scotland).

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Clements.—On November 21, 1953, at Poole, Dorset, to Sheila Mayer, wife of Dr. P. W. Clements, a daughter—Gillian Jane.

Gribble.—On November 28, 1953, at The London Hospital, London, E., to Mary (formerly Watkins), wife of Michael Gribble, B.M., B.Ch., a son—Julian de Gruchy.

Murley.—On November 30, 1953, at Cobden Hill House, Radlett, Herts, to Daphne (formerly Garrod), wife of Reginald S. Murley, M.S., F.R.C.S., a sister for Susan, Jennifer, David, and Gavin—Hilary.

MARRIAGES

Bird—Bateman.—On November 21, 1953, at Christ Church, Fulwood, Sheffield, Julian Davis Bird, M.B., Ch.B., D.A., to Nora Bateman, S.R.N., S.C.M.

Bowie—Whitfield.—On November 20, 1953, in London, William Wilson Bowie, M.B., Ch.B., D.Obst.R.C.O.G., to Enid Mary Whitfield, M.B., Ch.B., D.C.H.

DEATHS

Arthur.—On November 17, 1953, at Llandrindod Wells, Radnorshire, William Daniel Arthur, M.B.E., M.R.C.S., L.R.C.P., Colonel, late R.A.M.C., retired, of Llandaff, Cardiff.

Beetham.—On November 20, 1953, in hospital, Herbert William Beetham, L.R.C.P.&S.Ed., L.R.F.P.S., of 6, Lidgett Park Road, Leeds, Yorks, aged 46.

Ealand.—On November 11, 1953, Ralph Martin Ealand, M.R.C.S., L.R.C.P., late of Batheaston, Somerset.

Ellison.—On November 6, 1953, at the Grove Hospital, Tooting, London, S.W., Joseph Bramhall Ellison, M.D., D.P.H.

Hartley.—On November 6, 1953, at his home, 71, Lichfield Road, Sutton Coldfield, War, George Cleverdon Hartley, M.C., M.B., Ch.B., husband of Alice Muriel Hartley, M.B., Ch.B., formerly of Erdington, Birmingham, aged 66.

Hatch.—On November 16, 1953, Herbert Lincoln Hatch, M.B., B.S., D.P.H., of Pinner, Middlesex.

Henderson.—On November 14, 1953, at Bexhill-on-Sea, Sussex, Henry John Henderson, M.C., M.B., B.S., formerly of Amersham, Bucks.

Johnson.—On November 17, 1953, at Nearfield House, Bawtry, Yorks, Frederick Johnson, O.B.E., M.B., Ch.B., aged 77.

Latham.—On November 3, 1953, at 8, Ravenslea Road, Wandsworth Common, London, S.W., Donald Victor Latham, M.D., M.A.O., D.Obst.R.C.O.G., late of Grahamstown, South Africa, and Dar-es-Salaam, Tanganyika Territory, aged 56.

Lee.—On November 17, 1953, at 8, Glebe Road, Worthing, Sussex, Clifford Harry Lee, M.R.C.S., L.R.C.P., aged 57.

Macpherson.—On November 14, 1953, Charles Wattie Macpherson, M.B., Ch.B., of 277, Bramhall Lane South, Bramhall, Cheshire.

Nicholson.—On November 10, 1953, at Fairings, Finchampstead, Berks, Frederick Dering Nicholson, M.D.

Poole.—On November 11, 1953, at his home, 29, Balcombe Road, Horley, Surrey, Arthur Henry Poole, M.D., aged 86.

Prins.—On October 30, 1953, at his home, 315, Sheen Road, Richmond, Surrey, Lorenz Arthur Prins, I.S.O., L.R.C.P.&S.Ed., formerly of Colombo, Ceylon.

Robson.—On November 10, 1953, at Dar-es-Salaam, Tanganyika Territory, Thomas William Robson, M.R.C.S., L.R.C.P., formerly of Hazel Grove, Cheshire, aged 37.

Stone.—On November 9, 1953, at 30, Foxley Hill Road, Purley, Surrey, Ernest Richard Stone, M.B., B.Ch., D.T.M.

Woodwright.—On November 13, 1953, at his home, The Grove, Branksome Park, Bournemouth, Hants, William Henry Edward Woodwright, F.R.C.S.I., Lieutenant-Colonel, I.M.S., retired.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Frequent Defaecation

Q.—*A 40-year-old married man complains of symptoms which point to an unusually sensitive colon. Certain foods and drinks cause distressingly frequent defaecation. Among these are oatmeal, yeast extracts, malt, treacle, beer, and stout. These articles of diet do not in ordinary quantities produce loose stools, but they cause him to have anything from eight to twelve apparently normal motions a day. The complaint has troubled him since about the age of 18 years. What is the explanation of these symptoms?*

A.—The symptomatology described might have either a psychological or an organic basis. In either case, the simplest and best treatment would seem to be the avoidance of the offending articles of diet, provided that this does not lead to nutritional inadequacy. If it should be found impracticable, or deleterious to health, to restrict the diet in the way required, fuller investigation of the case is essential. If an organic basis can be clearly demonstrated—such as protein allergy, or inadequate digestion or absorption of some food material—appropriate corrective treatment should be instituted. If, however, no organic basis can be found, the advisability of psychotherapy must be considered.

When dietary restriction is practised, it is a good thing to examine the actual food intake quantitatively and in some detail; any likely deficiencies can then be corrected by appropriate supplementation.

Von Recklinghausen's Disease

Q.—*Have there been any recent advances in the treatment of von Recklinghausen's disease? Is it possible to form any estimate of the likely rate of progression in an individual case?*

A.—There have been no recent advances in the treatment of generalized neurofibromatosis (von Recklinghausen's disease). There are no special features which enable an estimate of the progression of the disease to be made.

Sedimentation Rate in Subacute Rheumatism

Q.—*How reliable is the erythrocyte sedimentation rate as an index of activity in subacute rheumatism?*

A.—The erythrocyte sedimentation rate is a valuable index of activity in subacute rheumatic fever, but, like all laboratory tests, it is not as reliable as clinical signs. It is seldom normal in the presence of physical signs. It may, however, be abnormally raised in the absence of clinical signs of rheumatic activity. In those circumstances it should be regarded as indicating a subclinical inflammatory process. Since in rheumatic fever the heart should be rested until all activity has subsided, it would be unwise to allow such patients to get up until the sedimentation rate has been within normal limits for at least 2–4 weeks, depending on whether the heart has previously been damaged. If there has been carditis in the acute attack, 4 weeks of bed rest, or sometimes even longer, is indicated *after the erythrocyte sedimentation rate has become normal.* The only exception to this generalization is in older girls, aged 14–20. In this age group sedimentation rates may remain high (say, 20–30 mm. per hour) for prolonged periods, often increasing at the menses, without any physical signs of activity or any adverse effects after letting the patient get up. It should be remembered that the erythrocyte sedimentation rate is a non-specific response and depends upon the presence in the body somewhere of an inflammatory process or tissue destruction, both of which lead to increased fibrinogen in

the plasma. The Wintrobe method sometimes gives anomalous results (readings which appear normal even with marked clinical signs of activity) and it is better to use the Westergren method, which gives readings more generally in accord with the clinical state.

Chapped Hands

Q.—*What is the most satisfactory treatment of the chapped hands so frequently seen in diabetics? As this condition is associated with cold weather, would the dry, cold climate of Alberta (Canada) aggravate the condition further?*

A.—The use of glycerin and rose water or some hand lotion containing glycerin is the most satisfactory treatment for chapping.

The condition appears to be dependent essentially upon the humidity of the atmosphere, which in cold weather is usually low. It is aggravated by winds, especially drying winds, usually from north and east, and by irritants such as soap and alkalis. If the humidity is low (indicated by a low dew-point) in Alberta, especially in cold weather, as seems probable, it would tend to provoke chapping.

Spasmodic Torticollis

Q.—*What treatment is advised for the spasms in a case of chronic spasmodic torticollis?*

A.—Spasmodic torticollis is most resistant to treatment. Medicinal treatment is of little value. Relaxation exercises and extension of the neck may be of temporary help. Immobilization of the cervical spine in plaster or in a plastic collar is often the most useful measure, though obviously in no way dealing with the unknown cause of the condition. Operative measures, in particular division of the upper cervical anterior roots, have been resorted to in some cases, but the results are by no means uniformly successful.

Switzerland for the Asthmatic

Q.—*What special advantages can Switzerland offer to asthmatic patients that are not available in Britain? Are any special types of asthmatic patient particularly likely to benefit from going there?*

A.—Switzerland has many obvious attractions for the British, but the particular advantage which it has to offer Britain's asthmatic patients is a climate far less conducive to infective changes in the respiratory tract. The death rate from bronchitis in England and Wales is 63.5 per 100,000 of the living population, while for Switzerland the figure is 6.8. The death rate from asthma in England and Wales is 7.0 per 100,000 and for Switzerland it is 4.2.

Changes of environment are known to benefit asthma when unsuspected allergens are thereby removed, when the psychological factors, also often unsuspected, are eliminated, or when the climate benefits the infective factor in asthma. All three types of asthma might indeed benefit by removal to Switzerland, but it is only for the infective type that one might claim that Switzerland, owing to its dry and warm climate, was particularly likely to result in improvement.

There is no reliable information whether asthmatic children do, in fact, do better in Switzerland than in Britain, and so far as the writer knows there are no means of getting asthmatic children to Switzerland on medical grounds to any form of institution. There is certainly no official scheme.

Tuberculosis in Paediatric Wards

Q.—*Should cases of tuberculous meningitis and miliary tuberculosis be treated in a children's ward? Is it safe to admit suspected cases of pulmonary tuberculosis to the ward, provided any found to be open are isolated at once?*

A.—If separate accommodation is available it is probably best not to treat cases of tuberculous meningitis and miliary tuberculosis in children's wards. Cases of tuberculous meningitis in particular are often exceedingly ill, and the meningitic cry may be very distressing to other patients. However, there is probably little risk of infection of other children as long as the patient does not have an adult type of pulmonary tuberculosis. Primary tuberculosis in children can be regarded for practical purposes as non-infective, although if such cases are treated in a ward with other children simple precautions should be observed, such as having separate crockery and linen.

Children with the adult type of pulmonary tuberculosis, with cavitation, should, of course, be excluded if possible, and isolated at once if they are diagnosed in the ward.

Lysozyme

Q.—*Is the antibacterial action of lysozyme in tears in any way comparable to that of the antibiotics? Has lysozyme any therapeutic possibilities?*

A.—Lysozyme was first isolated by Sir Alexander Fleming in 1922 in the secretion of the nasal mucosa. Subsequently it was found to be particularly plentiful in tears, but it is present also in many other tissues. Its antibacterial effect constitutes one of the defensive mechanisms of the body. The action of lysozyme is comparable to the antibiotics only because it is one of the many naturally occurring agents against bacteria. Its therapeutic efficacy is, however, low.

B.C.G. During Diphtheria-pertussis Immunization

Q.—*Would it be inadvisable to Mantoux test and give B.C.G. vaccination to a healthy child aged 16 months while he is undergoing immunization with a combined diphtheria-pertussis vaccine? The B.C.G. vaccination team will be in this district shortly, and I would like to know what to do.*

A.—This is a case where recommended procedure will depend to some extent on the child's environment. If it is known that the parents and other intimate contacts of the child are not suffering from open tuberculosis, and that the home and environmental conditions are such that the child is unlikely to be exposed to the risk of tuberculous infection, tuberculin testing and B.C.G. vaccination would not be regarded as an urgent measure. If, on the other hand, the chances of the child being exposed to tuberculosis are uncertain, it would be wise to test and vaccinate now when the opportunity presents, since the child is still at an age when tuberculous infection could be serious. Inoculation with the combined diphtheria-pertussis mixture, if it does not contain alum, is unlikely to cause much local or systemic reaction, and ordinarily there would be no contraindication to B.C.G. vaccination during the course of the other immunizations. If need be, the last injection of the combined prophylactic could be deferred for another month or more; and even if the B.C.G. vaccination is not done now it would be useful, and perfectly safe, to have the child tuberculin tested for future reference.

"Any Questions?" Book.—The second book of selected "Any Questions?" is available, price 7s. 6d. (postage 6d.). Copies may be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

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